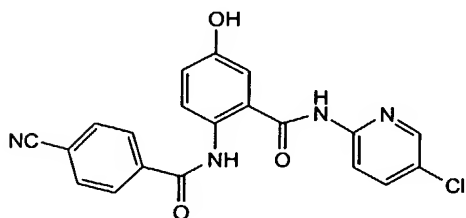


Example 282

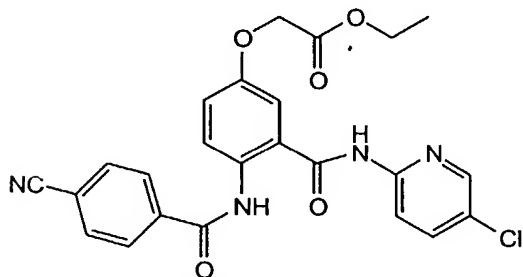
N-(5-chloro(2-pyridyl)){6-[(4-cyanophenyl)carbonylamino]-3-hydroxyphenyl}carboxamide



To a suspension of compound N-(5-chloro(2-pyridyl)){2-[(4-cyanophenyl)-carbonylamino]-5-methoxyphenyl}carboxamide (500mg, 1.2mmol) in DCM (100mL) at -78°C was added BBr₃ (2mL). The mixture was stirred at ambient temperatures for 72 hours. The solid was collected by filtration and was washed by DCM and water, dried under vacuum. The filtrate was concentrated and extracted with EtOAc. The organic extract was washed with brine, dried and evaporated. The resulting solid was combined with the solid obtained from filtration to give the title compound. Total yield is 90% (430mg). MS found for C₂₀H₁₃ClN₄O₃ (M+H)⁺: 393.0.

Example 283

ethyl 2-{3-[N-(5-chloro(2-pyridyl))carbonyl]-4-[(4-cyanophenyl)carbonylamino]-phenoxy}acetate



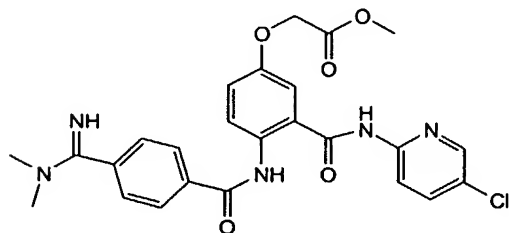
To a mixture of compound N-(5-chloro(2-pyridyl)){6-[(4-cyanophenyl)-carbonylamino]-3-hydroxyphenyl}carboxamide (50mg, 0.13mmol) and Cs₂CO₃

166

(83mg, 0.25mmol) in DMF (1mL) at room temperature was added ethyl bromoacetate (15μL, 0.13mmol). The mixture was stirred for 1 hour before diluted with EtOAc (20mL) and water (10mL). The organic layer was washed with brine dried and evaporated to give 70mg of the crude compound, which was used without farther
5 purification. MS found for $C_{24}H_{19}ClN_4O_5$ ($M+H$)⁺: 479.0.

Example 284

10 **methyl 2-[4-({4-[(dimethylamino)iminomethyl]phenyl}carbonylamino)-3-[N-(5-chloro(2-pyridyl))carbamoyl]phenoxy]acetate**



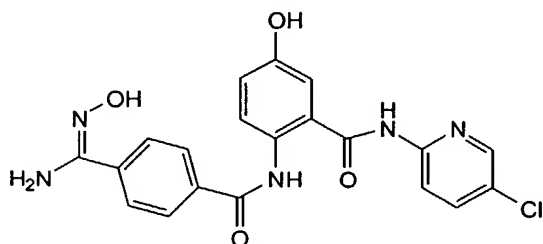
The title compound was obtained according to the procedure described Example 263.
MS found for $C_{25}H_{24}ClN_5O_5$ ($M+H$)⁺: 510.1.

15

Example 285

(6-{[4-(amino(hydroxyimino)methyl)phenyl]carbonylamino}-3-hydroxyphenyl)-N-(5-chloro(2-pyridyl))carboxamide

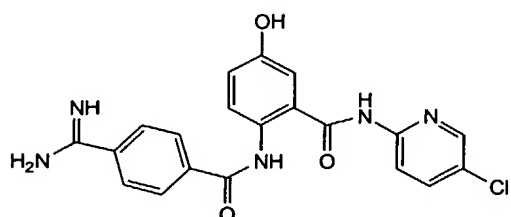
20



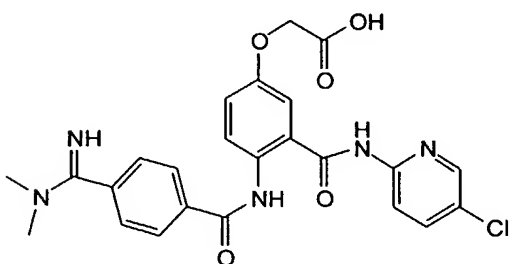
The title compound was obtained according to the procedure described in Example 270. MS found for $C_{20}H_{16}ClN_5O_4$ ($M+Na$)⁺: 448.0.

Example 286**4-(N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]-4-hydroxyphenyl}carbamoyl)-benzenecarboxamidine**

5



The title compound was obtained according to the procedure described in Example 282. MS found for $C_{20}H_{16}ClN_5O_3$ (M+H)⁺: 410.1.

10 Example 287**4-(N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]-4-hydroxyphenyl}carbamoyl)-benzenecarboxamidine**

15

To a solution of Example 284 (10mg) in MeOH (1mL) was added 50μL of 1N aq. LiOH solution. The mixture was stirred for 1 hour and purified by RP-HPLC to give the title compound. MS found for $C_{24}H_{22}ClN_5O_5$ (M+H)⁺: 496.

20

Without further description, it is believed that one of ordinary skill in the art can, using the preceding description and the illustrative examples, make and utilize the compounds of the present invention and practice the claimed methods. It should be understood that the foregoing discussion and examples merely present a detailed description

of certain preferred embodiments. It will be apparent to those of ordinary skill in the art that various modifications and equivalents can be made without departing from the spirit and scope of the invention. All the patents, journal articles and other documents discussed or cited above are herein incorporated by reference.

WHAT IS CLAIMED IS:

1. A compound of the following formula :



wherein:

5 A is selected from:

- (a) C_1-C_6 -alkyl;
 - (b) C_3-C_8 -cycloalkyl;
 - 10 (c) $-N(R^1, R^2)$, $N(R^1, R^2)-C(=NR^3)-$, $N(R^1, R^2)-C(=NR^3)-N(R^4)-$, $R^1-C(=NR^3)-$, $R^1-C(=NR^3)-N(R^4)-$;
 - (d) phenyl, which is independently substituted with 0-2 R substituents;
 - 15 (e) naphthyl, which is independently substituted with 0-2 R substituents;
- and
- a monocyclic or fused bicyclic heterocyclic ring system having from 5 to 10 ring atoms, wherein 1-4 ring atoms of the ring system are selected from N, O and S, and wherein the ring system may be
- 20 substituted with 0-2 R substituents;

R is selected from:

- H, halo, $-CN$, $-CO_2R^1$, $-C(=O)-N(R^1, R^2)$, $-(CH_2)_m-CO_2R^1$, $-(CH_2)_m-$
 $C(=O)-N(R^1, R^2)$, $-NO_2$, $-SO_2N(R^1, R^2)$, $-SO_2R^1$, $-(CH_2)_mNR^1R^2$, $-(CH_2)_m-$
 25 $C(=NR^3)-R^1$, $-(CH_2)_m-C(=NR^3)-N(R^1, R^2)$, $-(CH_2)_m-N(R^4)-C(=NR^3)-N(R^1, R^2)$, $-(CH_2)_mNR^1-$ group appended to a 3 to 6 membered heterocyclic ring containing from 1-4 heteroatoms selected from N, O and S, $-C_{1-4}alkyl$, $-C_{2-6}alkenyl$, $-C_{2-6}alkynyl$, $-C_{3-8}cycloalkyl$, $-C_{0-4}alkylC_{3-8}cycloalkyl$, $-CF_3$, $-OR^2$, and a 5-6
 30 membered heterocyclic system containing from 1-4 heteroatoms selected from N, O and S, wherein from 1-4 hydrogen atoms on the heterocyclic system may be independently replaced with a member selected from the group consisting of halo, $-C_1-C_4-alkyl$, $-C_{1-4}alkyl-CN$, $-C_{2-6}alkenyl$, $-C_{2-6}alkynyl$, $-C_{3-8}cycloalkyl$, $-C_{0-4}alkylC_{3-8}cycloalkyl$ and $-NO_2$;

m is an integer of 0-2;

R¹, R², R³ and R⁴ are independently selected from the group consisting of:

5 H, -OR⁵, -N(-R⁵, -R⁶), -C₁₋₄alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₄alkylC₃₋₈cycloalkyl, -C₀₋₄alkylphenyl and -C₀₋₄alkylnaphthyl, wherein from 1-4 hydrogen atoms on the ring atoms of the phenyl and naphthyl moieties may be independently replaced with a member selected from the group consisting of halo, -C₁₋₄alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₄alkylC₃₋₈cycloalkyl, -CN, and -NO₂; or

10

R¹ and R², or R² and R³ taken together can form a 3-8 membered cycloalkyl or a heterocyclic ring system, wherein the heterocyclic ring system may have from 3 to 10 ring atoms, with 1 to 2 rings being in the ring system and contain from 1-4 heteroatoms selected from N, O and S, wherein from 1-4 hydrogen atoms on the heterocyclic ring system may be independently replaced with a member selected from the group consisting of halo, C₁-C₄-alkyl, -CN -C₁₋₄alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₄alkylC₃₋₈cycloalkyl and -NO₂;

15

20 R⁵ and R⁶ are independently selected from the group consisting of:

H, -C₁₋₄alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₄alkylC₃₋₈cycloalkyl, -C₀₋₄alkylphenyl and -C₀₋₄alkylnaphthyl, wherein from 1-4 hydrogen atoms on the ring atoms of the phenyl and naphthyl moieties may be independently replaced with a member selected from the group consisting of halo, -C₁₋₄alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₄alkylC₃₋₈cycloalkyl, -CN, and -NO₂; or

25

R⁵ and R⁶ taken together can form a 3-8 membered cycloalkyl or a heterocyclic ring system, wherein the heterocyclic ring system may have from 3 to 10 ring atoms, with 1 to 2 rings being in the ring system and contain from 1-4 heteroatoms selected from N, O and S, wherein from 1-4 hydrogen atoms on the heterocyclic ring system may be independently replaced with a member selected from the group consisting of halo, -C₁-C₄-alkyl, -CN -C₁₋₄alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₄alkylC₃₋₈cycloalkyl and -NO₂;

30

35

Q is a member selected from the group consisting of:

a direct link, $-\text{CH}_2-$, $-\text{C}(=\text{O})-$, $-\text{O}-$, $-\text{N}(\text{R}^7)-$, $-\text{N}(\text{R}^7)\text{CH}_2-$, $-\text{CH}_2\text{N}(\text{R}^7)-$, $-\text{C}(=\text{NR}^7)-$, $-\text{C}(=\text{O})-\text{N}(\text{R}^7)-$, $-\text{N}(\text{R}^7)-\text{C}(=\text{O})-$, $-\text{S}-$, $-\text{SO}-$, $-\text{SO}_2-$, $-\text{SO}_2-\text{N}(\text{R}^7)-$ and $-\text{N}(\text{R}^7)-\text{SO}_2-$;

5 R^7 is selected from:

H, $-\text{C}_{1-4}\text{alkyl}$, $-\text{C}_{2-6}\text{alkenyl}$, $-\text{C}_{2-6}\text{alkynyl}$, $-\text{C}_{3-8}\text{cycloalkyl}$, $-\text{C}_{0-4}\text{alkylC}_{3-8}\text{cycloalkyl}$, $-\text{C}_{0-4}\text{alkylphenyl}$ and $-\text{C}_{0-4}\text{alkylnaphthyl}$, wherein from 1-4 hydrogen atoms on the ring atoms of the phenyl and naphthyl moieties may be independently replaced with a member selected from the group consisting of
 10 halo, $-\text{C}_{1-4}\text{alkyl}$, $-\text{C}_{2-6}\text{alkenyl}$, $-\text{C}_{2-6}\text{alkynyl}$, $-\text{C}_{3-8}\text{cycloalkyl}$, $-\text{C}_{0-4}\text{alkylC}_{3-8}\text{cycloalkyl}$, $-\text{CN}$, and $-\text{NO}_2$;

D is a direct link or is a member selected from the group consisting of:

- (a) phenyl, which is independently substituted with 0-2 R^{1a} substituents;
 15 (b) naphthyl, which is independently substituted with 0-2 R^{1a} substituents; and
 (c) a monocyclic or fused bicyclic heterocyclic ring system having from 5 to 10 ring atoms, wherein 1-4 ring atoms of the ring system are selected from N, O and S, and wherein the ring system may be
 20 substituted from 0-2 R^{1a} substituents;

R^{1a} is selected from:

halo, $-\text{C}_{1-4}\text{alkyl}$, $-\text{C}_{2-6}\text{alkenyl}$, $-\text{C}_{2-6}\text{alkynyl}$, $-\text{C}_{3-8}\text{cycloalkyl}$, $-\text{C}_{0-4}\text{alkylC}_{3-8}\text{cycloalkyl}$, $-\text{CN}$, $-\text{NO}_2$, $-(\text{CH}_2)_n\text{NR}^{2a}\text{R}^{3a}$, $-(\text{CH}_2)_n\text{CO}_2\text{R}^{2a}$, $-(\text{CH}_2)_n\text{CONR}^{2a}\text{R}^{3a}$,
 25 $-\text{SO}_2\text{NR}^{2a}\text{R}^{3a}$, $-\text{SO}_2\text{R}^{2a}$, $-\text{CF}_3$, $-\text{OR}^{2a}$, and a 5-6 membered aromatic heterocyclic system containing from 1-4 heteroatoms selected from N, O and S, wherein from 1-4 hydrogen atoms on the aromatic heterocyclic system may be independently replaced with a member selected from the group consisting of
 30 halo, $-\text{C}_{1-4}\text{alkyl}$, $-\text{C}_{2-6}\text{alkenyl}$, $-\text{C}_{2-6}\text{alkynyl}$, $-\text{C}_{3-8}\text{cycloalkyl}$, $-\text{C}_{0-4}\text{alkylC}_{3-8}\text{cycloalkyl}$, $-\text{CN}$ and $-\text{NO}_2$;

R^{2a} and R^{3a} are independently selected from the group consisting of:

H, $-\text{C}_{1-4}\text{alkyl}$, $-\text{C}_{2-6}\text{alkenyl}$, $-\text{C}_{2-6}\text{alkynyl}$, $-\text{C}_{3-8}\text{cycloalkyl}$, $-\text{C}_{0-4}\text{alkylC}_{3-8}\text{cycloalkyl}$, $-\text{C}_{0-4}\text{alkylphenyl}$ and $-\text{C}_{0-4}\text{alkylnaphthyl}$, wherein from 1-4
 35 hydrogen atoms on the ring atoms of the phenyl and naphthyl moieties may be

independently replaced with a member selected from the group consisting of halo, $-C_{1-4}$ alkyl, $-C_{2-6}$ alkenyl, $-C_{2-6}$ alkynyl, $-C_{3-8}$ cycloalkyl, $-C_{0-4}$ alkyl C_{3-8} cycloalkyl, $-CN$ and $-NO_2$;

5 n is an integer of 0-2;

E is a direct link or a member selected from the group consisting of:

$-C_{1-2}$ alkyl-, $-O-$, $-S-$, $-SO-$, $-SO_2-$, $-C_{0-1}$ alkyl- $C(=O)-$, $-C_{0-1}$ alkyl- $C(=O)-N(-R^8)-$
 C_{0-1} alkyl-, $-C_{0-1}$ alkyl- $N(-R^8)-C(=O)-C_{0-1}$ alkyl-, $-N(-R^8)-C(=O)-N(-R^8)-$ and
 10 $-C_{0-1}$ alkyl- $N(-R^8)-$;

R^8 is a member selected from the group consisting of:

H; $-C_{1-4}$ alkyl; $-C_{0-4}$ alkylaryl; $-C_{0-4}$ alkyl-heteroaryl; $-C_{1-4}$ alkyl- $C(=O)-OH$,
 $-C_{1-4}$ alkyl- $C(=O)-O-C_{1-4}$ alkyl, and $-C_{1-4}$ alkyl- $C(=O)-N(-R^{2b}, -R^{3b})$;

15

R^{2b} and R^{3b} are each a member independently selected from the group consisting of:

H, $-C_{1-4}$ alkyl, $-C_{0-4}$ alkyl-aryl; $-C_{0-4}$ alkyl-heterocyclic group, and R^{2b} and R^{3b}
 together with the N atom to which they are attached can form a 5-8 membered
 heterocyclic ring containing 1-4 heteroatoms selected from N, O and S,
 20 wherein the heterocyclic ring may be substituted with 0-2 R^{1c} groups;

R^{1c} is a member selected from the group consisting of:

Halo; $-C_{1-4}$ alkyl; $-CN$, $-NO_2$; $-C(=O)-N(-R^{2c}, -R^{3c})$; $-C(=O)-OR^{2c}$;
 $-(CH_2)_q-N(-R^{2c}, -R^{3c})$; $-SO_2-N(-R^{2c}, -R^{3c})$; $-SO_2R^{2c}$; $-CF_3$ and $-(CH_2)_q-OR^{2c}$;

25

R^{2c} and R^{3c} are each independently a member selected from the group consisting of:

H; $-C_{1-4}$ alkyl and $-C_{1-4}$ alkyl-aryl;

q is an integer of 0-2;

30

G is a member selected from the group consisting of:

(a) C_2 -alkenyl or C_{3-8} -cycloalkenyl, wherein the alkenyl and cycloalkenyl
 attachment points are the alkenyl carbon atoms and wherein the $-C_2$ -
 alkenyl or $-C_{3-8}$ -cycloalkenyl are substituted with 0-4 R^{1d} groups;

35

- (b) a phenylene group wherein the ring carbon atoms of the phenylene group are substituted with 0-4 R^{1d} groups;
- (c) a 3-8 membered a saturated, partially unsaturated or aromatic monocyclic- heterocyclic ring system containing 1-4 heteroatoms selected from N, O and S, wherein 0-2 ring atoms of the heterocyclic ring may be substituted with 0-4 R^{1d} groups; and,
- (d) an 8-10 membered fused heterocyclic bicyclic ring system, containing 1-4 heteroatoms selected from N, O and S, wherein 0-2 ring atoms of the fused bicyclic ring system may be substituted with 0-4 R^{1d} groups;

R^{1d} is a member selected from the group consisting of:

- H, halo; C_{1-6} -alkyl, carbocyclic aryl, -CN; -NO₂; -(CH₂)₀₋₆-NR^{2d}R^{3d};
 -SO₂NR^{2d}R^{3d}; -SO₂R^{2d}; -CF₃; -(CH₂)₀₋₆-OR^{2d}; -O-(CH₂)₁₋₆OR^{2d}; -O-(CH₂)₁₋₆-C(=O)-O-R^{2d};
 -O-(CH₂)₁₋₆-C(=O)-N(R^{2d},R^{3d}); -N(R^{5a})-(CH₂)₁₋₆-OR^{2d};
 -N(R^{5a})-(CH₂)₁₋₆-N(R^{2d},R^{3d}); -C(=O)-N(R^{2d},R^{3d});
 -N(R^{5a})-(CH₂)₁₋₆-C(=O)-N(R^{2d},R^{3d}); -N(-(CH₂)₁₋₆-OR^{2d})₂; -N(R^{5a})-(CH₂)₁₋₆-OR^{2d};
 -N(R^{5a})-C(=O)-R^{2d}; -N(R^{5a})-SO₂-R^{2d}; -(CH₂)₀₋₆-C(=O)-O-R^{2d}; -(CH₂)₀₋₆-C(=O)-N(R^{2d},R^{3d});
 -(CH₂)₀₋₆-C(=NR^{2d})-N(R^{3d},R^{4d}); -(CH₂)₀₋₆-N(R^{5a})C(=NR^{2d})-N(R^{3d},R^{4d}); a -(CH₂)₀₋₆-N(R^{3d})C₅₋₆ membered saturated, partially unsaturated or aromatic heterocyclic ring containing 1-4 heteroatoms selected from N, O and S, and a -(CH₂)₀₋₆-5-6 membered saturated, partially unsaturated or aromatic heterocyclic ring containing 1-4 heteroatoms selected from N, O and S;

R^{5a} , R^{2d} , R^{3d} and R^{4d} are each independently a member selected from the group consisting of:

- H, C_{1-6} -alkyl and C_{1-6} -alkylaryl, -CN; -NO₂; carbocyclic aryl, -CN; -NO₂; or

R^{2d} and R^{3d} taken together with the N atoms they are independently attached form a 5-7 membered saturated, partially unsaturated or aromatic heterocyclic ring; or

R^{3d} and R^{4d} taken together with the N atom to which they are attached form a 5-8 membered saturated, partially unsaturated or aromatic heterocyclic ring containing 1-4 heteroatoms selected from N, O and S;

- 5 J is a direct link or is a member selected from the group consisting of:
 $-N(-R^9)-C(=O)-$; $-C(=O)-N(-R^9)-$; $-O-$; $-S-$; $-SO-$; $-SO_2-$; $-CH_2-$; $-N(-R^9)-$; and
 $-N(-R^9)-SO_2-$;

R^9 is a member selected from the group consisting of:

- 10 H; $-C_{1-4}$ -alkyl; $-C_{0-4}$ -alkyl-carbocyclic aryl; $-(CH_2)_{0-4}$ -5-6 membered saturated, partially unsaturated or aromatic heterocyclic ring containing 1-4 heteroatoms selected from N, O and S; $-(CH_2)_{1-6}-C(=O)-O-C_{1-4}$ -alkyl; and $-(CH_2)_1$ - $_6-C(=O)-N(R^{6a}, R^{6b})$;

- 15 R^{6a} and R^{6b} are each a member independently selected from the group consisting of:
H and $-C_{1-6}$ -alkyl;

X is a member selected from the group consisting of:

- (a) phenyl substituted with 0-3 R^{1e} groups;
20 (b) naphthyl substituted with 0-3 R^{1e} groups and
(c) a 6-membered aromatic heterocyclic ring system containing 1-3 N atoms and having 0-3 ring atoms substituted with 0-3 R^{1e} groups; and
25 (d) an 8-10 membered fused aromatic heterocyclic bicyclic ring system containing 1-4 heteroatoms selected from N, O and S and 0-3 ring atoms of the fused heterocyclic bicyclic ring system are substituted with 0-3 R^{1e} groups;

30

R^{1e} is a member independently selected from the group consisting of:

- Halo; CF_3 ; $-C_{1-4}$ -alkyl; carbocyclic aryl; $-C_{0-2}$ -alkyl-CN; $-O-R^{2e}$;
 $-C_{0-2}$ -alkyl- $C(=O)-O-R^{2e}$; $-C_{0-2}$ -alkyl- $C(=O)-N(R^{2e}, R^{3e})$; $-C_{0-2}$ -alkyl- NO_2 ;
 $-C_{0-2}$ -alkyl- $N(R^{2e}, R^{3e})$; $-C_{0-2}$ -alkyl- $SO_2-N(R^{2e}, R^{3e})$; $-C_{0-2}$ -alkyl- SO_2-R^{2e} ;
35 trihaloalkyl; $-O-C_{0-2}$ -alkyl- $O-R^{2e}$; $-C_{0-2}$ -alkyl- $O-R^{2e}$; $-O-C_{1-4}$ -alkyl-

$C(=O)-N(R^{2e}, R^{3e})$; $-O-C_{1-4}-alkyl-C(=O)-O-R^{2e}$; $-C_{0-2}-alkyl-N(R^{2e})-C(=O)-R^{3e}$;
 $-C_{0-2}-alkyl-N(-R^{2e})-SO_2-R^{3e}$; $-CH_2-N(R^{2e})-C(=O)-R^{3e}$; $-CH_2-N(R^{2e})-SO_2-R^{3e}$;
 $-(CH_2)_{0-6}-NR^{2e}R^{3e}$; $-C(=O)-N(R^{2e}, R^{3e})$; $-N(-(CH_2)_{1-6}-OR^{2e})_2$; $-N(R^{10})-(CH_2)_{1-6}-OR^{2e}$;
 $-N(R^{10})-C(=O)-R^{2e}$; $-N(R^{10})-SO_2-R^{2e}$; $-C(=N(R^{10}))-N(R^{2e}, R^{3e})$; and a
 5 $-(CH_2)_{0-6}$ -5-6 membered saturated, partially unsaturated or aromatic heterocyclic ring containing 1-4 heteroatoms selected from N, O and S;

R^{10} , R^{2e} and R^{3e} are each independently a member selected from the group consisting of:

10 H; $-C_{1-4}-alkyl$; $-C_{0-2}-alkyl-O-R^{1g}$; $-C_{0-2}-alkyl-N(-R^{1g}, -R^{2g})$; $-C_{1-4}-alkyl-carbocyclic\ aryl$; $-C_{1-4}-alkyl-heterocyclic$; and R^{10} and R^{2e} , or R^{2e} and R^{3e} together with the N atom to which they are attached can form 5-8 membered heterocyclic ring containing 1-4 heteroatoms selected from N, O and S which can be substituted with 0-2 R^{1g} groups;

15

R^{1g} and R^{2g} are independently a member selected from the group of:

H; halo; $-C_{1-4}-alkyl$, a carbocyclic aryl group; a saturated, partially unsaturated or aromatic heterocyclic group; $-CN$; $-C(=O)-N(R^{3g})R^{4g}$; $-C(=O)-OR^{3g}$; $-NO_2$;
 $-(CH_2)_p-NR^{3g}R^{4g}$; $-SO_2NR^{3g}R^{4g}$; $-SO_2R^{3g}$; $-CF_3$; and $-(CH_2)_pOR^{3g}$;

20

p is an integer of 0-2;

R^{3g} and R^{4g} are each independently selected from the group consisting of:

H; $-C_{1-4}-alkyl$ and $-C_{0-4}-alkyl-carbocyclic\ aryl$;

25

and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

2. A compound of claim 1, wherein:

30 A is selected from:

(a) $C_1-C_6-alkyl$;

(b) $C_3-C_8-cycloalkyl$;

- (c) $-N(R^1, R^2)$, $N(R^1, R^2)-C(=NR^3)-$, $N(R^1, R^2)-C(=NR^3)-N(R^4)-$, $R^1-C(=NR^3)-$, $R^1-C(=NR^3)-N(R^4)-$;
- (d) phenyl, which is independently substituted with 0-2 R substituents;
- (e) naphthyl, which is independently substituted with 0-2 R substituents;
- and
- (f) monocyclic or fused bicyclic heterocyclic ring system having from 5 to 10 ring atoms, wherein 1-4 ring atoms of the ring system are selected from N, O and S, and wherein the ring system may be substituted with 0-2 R substituents;

R is selected from:

- H, halo, $-CN$, $-CO_2R^1$, $-C(=O)-N(R^1, R^2)$, $-(CH_2)_m-CO_2R^1$, $-(CH_2)_m-C(=O)-N(R^1, R^2)$, $-NO_2$, $-SO_2N(R^1, R^2)$, $-SO_2R^1$, $-(CH_2)_mNR^1R^2$, $-(CH_2)_m-C(=NR^3)-R^1$, $-(CH_2)_m-C(=NR^3)-N(R^1, R^2)$, $-(CH_2)_m-N(R^4)-C(=NR^3)-N(R^1, R^2)$, $-(CH_2)_mNR^1$ - group attached to a 3-6 membered heterocyclic ring having from 1 to 3 heteroatoms selected from the group consisting of N, O and S, $-C_{1-4}alkyl$, $-C_{2-6}alkenyl$, $-C_{2-6}alkynyl$, $-C_{3-8}cycloalkyl$, $-C_{0-4}alkylC_{3-8}cycloalkyl$, $-CF_3$, $-OR^2$, and a 5-6 membered heterocyclic aromatic or partially saturated system, including imidazoline, containing from 1-4 heteroatoms selected from N, O and S, wherein from 1-4 hydrogen atoms on the heterocyclic system may be independently replaced with a member selected from the group consisting of
- halo, methyl, $-C_2-C_4-alkyl$, $-CN$, $-C_{2-6}alkenyl$, $-C_{2-6}alkynyl$, $-C_{3-8}cycloalkyl$, $-C_{0-4}alkylC_{3-8}cycloalkyl$ and $-NO_2$;

m is an integer of 0-2;

- R^1 , R^2 , R^3 and R^4 are independently selected from the group consisting of:
- H, $-OR^5$, $-N(-R^5, -R^6)$, $-C_{1-4}alkyl$, $-C_{2-6}alkenyl$, $-C_{2-6}alkynyl$, $-C_{3-8}cycloalkyl$, $-C_{0-4}alkylC_{3-8}cycloalkyl$, $-C_{0-4}alkylphenyl$ and $-C_{0-4}alkylnaphthyl$, wherein from 1-4 hydrogen atoms on the ring atoms of the phenyl and naphthyl moieties may be independently replaced with a member selected from the group

consisting of halo, -C₁₋₄alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₄alkylC₃₋₈cycloalkyl, -CN, and -NO₂; or

5 R¹ and R², or R² and R³ taken together can form a 3-8 membered cycloalkyl or a heterocyclic ring system, wherein the heterocyclic ring system may have from 3 to 10 ring atoms, with 1 to 2 rings being in the ring system and contain from 1-4 heteroatoms selected from N, O and S, wherein from 1-4 hydrogen atoms on the heterocyclic ring system may be independently replaced with a member selected from the group consisting of halo, C₁-C₄-alkyl, -CN -C₁₋₄alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₄alkylC₃₋₈cycloalkyl and -NO₂;

R⁵ and R⁶ are independently selected from the group consisting of:

15 H, -C₁₋₄alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₄alkylC₃₋₈cycloalkyl, -C₀₋₄alkylphenyl and -C₀₋₄alkylnaphthyl, wherein from 1-4 hydrogen atoms on the ring atoms of the phenyl and naphthyl moieties may be independently replaced with a member selected from the group consisting of halo, -C₁₋₄alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₄alkylC₃₋₈cycloalkyl, -CN, and -NO₂; or

20 R⁵ and R⁶ taken together can form a 3-8 membered cycloalkyl or a heterocyclic ring system, wherein the heterocyclic ring system may have from 3 to 10 ring atoms, with 1 to 2 rings being in the ring system and contain from 1-4 heteroatoms selected from N, O and S, wherein from 1-4 hydrogen atoms on the heterocyclic ring system may be independently replaced with a member selected from the group consisting of halo, C₁-C₄-alkyl, -CN -C₁₋₄alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₄alkylC₃₋₈cycloalkyl and -NO₂;

Q is a member selected from the group consisting of:

30 a direct link, -CH₂-, -C(=O)-, -O-, -NH-, -NMe-, -NHCH₂-, -NMeCH₂-, -CH₂NH-, -C(=NH)-, -C(=O)-NH-, -NH-C(=O)-, -CH₂NMe-, -C(=NMe)-;

D is a direct link or is a member selected from the group consisting of:

35 (a) phenyl, which is independently substituted with 0-2 R^{1a} substituents;

(b) naphthyl, which is independently substituted with 0-2 R^{1a} substituents; and

5 a monocyclic or fused bicyclic heterocyclic ring system having from 5 to 10 ring atoms, wherein 1-4 ring atoms of the ring system are selected from N, O and S, and wherein the ring system may be substituted from 0-2 R^{1a} substituents;

R^{1a} is selected from:

10 halo, -C₁₋₄alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₄alkylC₃₋₈cycloalkyl, -CN, -NO₂, -(CH₂)_nNR^{2a}R^{3a}, -(CH₂)_nCO₂R^{2a}, -(CH₂)_nCONR^{2a}R^{3a}, -SO₂NR^{2a}R^{3a}, -SO₂R^{2a}, -CF₃, -OR^{2a}, and a 5-6 membered aromatic heterocyclic system containing from 1-4 heteroatoms selected from N, O and S, wherein from 1-4 hydrogen atoms on the aromatic heterocyclic system may be independently replaced with a member selected from the group consisting of

15 halo, -C₁₋₄alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₄alkylC₃₋₈cycloalkyl, -CN and -NO₂;

R^{2a} and R^{3a} are independently selected from the group consisting of:

20 H, -C₁₋₄alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₄alkylC₃₋₈cycloalkyl, -C₀₋₄alkylphenyl and -C₀₋₄alkylnaphthyl, wherein from 1-4 hydrogen atoms on the ring atoms of the phenyl and naphthyl moieties may be independently replaced with a member selected from the group consisting of halo, -C₁₋₄alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₄alkylC₃₋₈cycloalkyl, -CN and -NO₂;

25

n is an integer of 0-2;

E is a member selected from the group consisting of:

30 a direct link, -O-, -NH-, -CH₂NH-, -NHCH₂-, -NMe-, -NH-C(=O)-NH-, -C(=O)-NH-, -NH-C(=O)-;

G is a member selected from the group consisting of:

(a) a C₂-alkenyl group or a C₃₋₈-cycloalkenyl group, wherein the alkenyl group and cycloalkenyl group attachment points are the alkenyl carbon

atoms and wherein the C₂-alkenyl group or C₃₋₈-cycloalkenyl group is substituted with 0-4 R^{1d} groups;

- 5 (b) a phenylene group wherein the ring carbon atoms of the phenylene group are substituted with 0-4 R^{1d} groups;
- (c) a 3-8 membered a saturated, partially unsaturated or aromatic monocyclic- heterocyclic ring system containing 1-4 heteroatoms selected from N, O and S, wherein 0-4 ring atoms of the heterocyclic ring may be substituted with 0-4 R^{1d} groups; and,
- 10 (d) an 8-10 membered fused heterocyclic bicyclic ring system, containing 1-4 heteroatoms selected from N, O and S, wherein 0-4 ring atoms of the fused bicyclic ring system may be substituted with 0-4 R^{1d} groups;

15

R^{1d} is a member selected from the group consisting of:

- H, halo; C₁₋₆-alkyl, carbocyclic aryl, -CN; -NO₂; -(CH₂)₀₋₆-NR^{2d}R^{3d},
 -SO₂NR^{2d}R^{3d}; -SO₂R^{2d}; -CF₃; -(CH₂)₀₋₆-OR^{2d}; -O-(CH₂)₁₋₆OR^{2d}; -O-(CH₂)₁₋₆-C(=O)-O-R^{2d};
 20 -O-(CH₂)₁₋₆-C(=O)-N(R^{2d},R^{3d}); -N(R^{5a})-(CH₂)₁₋₆-OR^{2d},
 -N(R^{5a})-(CH₂)₁₋₆-N(R^{2d},R^{3d}); -C(=O)-N(R^{2d},R^{3d});
 -N(R^{5a})-(CH₂)₁₋₆-C(=O)-N(R^{2d},R^{3d}); -N(-(CH₂)₁₋₆-OR^{2d})₂; -N(R^{5a})-(CH₂)₁₋₆-OR^{2d};
 -N(R^{5a})-C(=O)-R^{2d}; -N(R^{5a})-SO₂-R^{2d}; -(CH₂)₀₋₆-C(=O)-O-R^{2d}; -(CH₂)₀₋₆-C(=O)-N(R^{2d},R^{3d}); -(CH₂)₀₋₆-C(=NR^{2d})-N(R^{3d},R^{4d});
 25 -(CH₂)₀₋₆-N(R^{5a})C(=NR^{2d})-N(R^{3d},R^{4d}); and a -(CH₂)₀₋₆-N(R^{3d}) group which is attached via the nitrogen atom to a carbon atom of a 5 to 6 membered saturated, partially unsaturated or aromatic heterocyclic ring containing 1-4 heteroatoms selected from N, O and S, and a -(CH₂)₀₋₆- group attached to a 5-6 membered saturated, partially unsaturated or aromatic heterocyclic ring
 30 containing 1-4 heteroatoms selected from N, O and S;

R^{5a}, R^{2d}, R^{3d} and R^{4d} are each independently a member selected from the group consisting of:

- 35 H, C₁₋₆-alkyl and C₁₋₆-alkylaryl, -CN; -NO₂; carbocyclic aryl, -CN; -NO₂; or

R^{2d} and R^{3d} taken together with the N atoms they are independently attached form a 5-7 membered saturated, partially unsaturated or aromatic heterocyclic ring; or

- 5 R^{3d} and R^{4d} taken together with the N atom to which they are attached form a 5-8 membered saturated, partially unsaturated or aromatic heterocyclic ring containing 1-4 heteroatoms selected from N, O and S;

J is a member selected from the group consisting of:

- 10 a direct link, -O-, -NH-, -NMe-, -C(=O)-NH-, -NH-C(=O)-;

X is a member selected from the group consisting of:

- (a) phenyl substituted with 0-3 R^{1e} groups;
- 15 (b) naphthyl substituted with 0-3 R^{1e} groups and
- (c) a 6-membered aromatic heterocyclic ring system containing 1-3 N atoms and having 0-3 ring atoms substituted with 0-3 R^{1e} groups; and
- 20 (d) an 8-10 membered fused aromatic heterocyclic bicyclic ring system containing 1-4 heteroatoms selected from N, O and S and 0-3 ring atoms of the fused heterocyclic bicyclic ring system are substituted with 0-3 R^{1e} groups;

- 25 R^{1e} is a member independently selected from the group consisting of:

Halo; CF_3 ; $-C_{1-4}$ -alkyl; carbocyclic aryl; $-C_{0-2}$ -alkyl-CN; $-O-R^{2e}$; $-C_{0-2}$ -alkyl-C(=O)-O- R^{2e} ; $-C_{0-2}$ -alkyl-C(=O)-N(R^{2e} , R^{3e}); $-C_{0-2}$ -alkyl-NO₂; $-C_{0-2}$ -alkyl-N(R^{2e} , R^{3e}); $-C_{0-2}$ -alkyl-SO₂-N(R^{2e} , R^{3e}); $-C_{0-2}$ -alkyl-SO₂- R^{2e} ; trihaloalkyl; $-O-C_{0-2}$ -alkyl-O- R^{2e} ; $-C_{0-2}$ -alkyl-O- R^{2e} ; $-O-C_{1-4}$ -alkyl-C(=O)-N(R^{2e} , R^{3e}); $-O-C_{1-4}$ -alkyl-C(=O)-O- R^{2e} ; $-C_{0-2}$ -alkyl-N(R^{2e})-C(=O)- R^{3e} ; $-C_{0-2}$ -alkyl-N(R^{2e})-SO₂- R^{3e} ; $-CH_2$ -N(R^{2e})-C(=O)- R^{3e} ; $-CH_2$ -N(R^{2e})-SO₂- R^{3e} ; $-(CH_2)_{0-6}$ -NR^{2e}R^{3e}; $-C(=O)$ -N(R^{2e} , R^{3e}); $-N(-(CH_2)_{1-6}-OR^{2e})_2$; $-N(R^{10})-(CH_2)_{1-6}-OR^{2e}$; $-N(R^{10})-C(=O)-R^{2e}$; $-N(R^{10})-SO_2-R^{2e}$; $-C(=N(R^{10}))$ -N(R^{2e} , R^{3e}); and a $-(CH_2)_{0-5}$ -6 membered saturated, partially unsaturated or aromatic heterocyclic ring containing 1-4 heteroatoms selected from N, O and S;

30

35

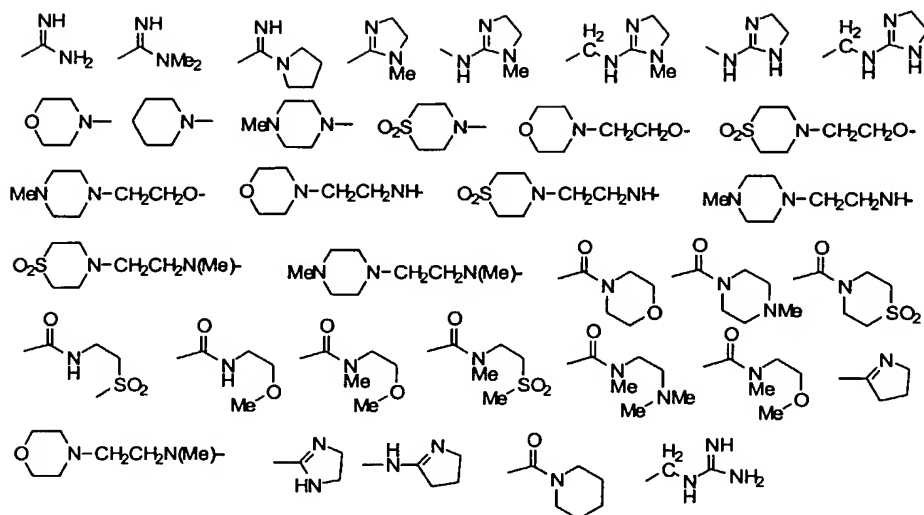
R^{10} , R^{2e} and R^{3e} are each independently a member selected from the group consisting of:

- 5 H; $-C_{1-4}$ -alkyl; $-C_{0-2}$ -alkyl-O- R^{1g} ; $-C_{0-2}$ -alkyl-N($-R^{1g}$, $-R^{2g}$); $-C_{1-4}$ -alkyl-carbocyclic aryl; $-C_{1-4}$ -alkyl-heterocyclic; and R^{10} and R^{2e} , or R^{2e} and R^{3e} together with the N atom to which they are attached can form 5-8 membered heterocyclic ring containing 1-4 heteroatoms selected from N, O and S which can be substituted with 0-2 R^{1g} groups;
- 10 R^{1g} and R^{2g} are independently a member selected from the group of:
 H; halo; $-C_{1-4}$ -alkyl, a carbocyclic aryl group; a saturated, partially unsaturated or aromatic heterocyclic group; $-\text{CN}$; $-\text{C}(=\text{O})-\text{N}(\text{R}^{3g}, \text{R}^{4g})$; $-\text{C}(=\text{O})-\text{OR}^{3g}$; $-\text{NO}_2$; $-(\text{CH}_2)_p-\text{NR}^{3g}\text{R}^{4g}$; $-\text{SO}_2\text{NR}^{3g}\text{R}^{4g}$; $-\text{SO}_2\text{R}^{3g}$; $-\text{CF}_3$; and $-(\text{CH}_2)_p\text{OR}^{3g}$;
- 15 p is an integer of 0-2;

R^{3g} and R^{4g} are each independently selected from the group consisting of:

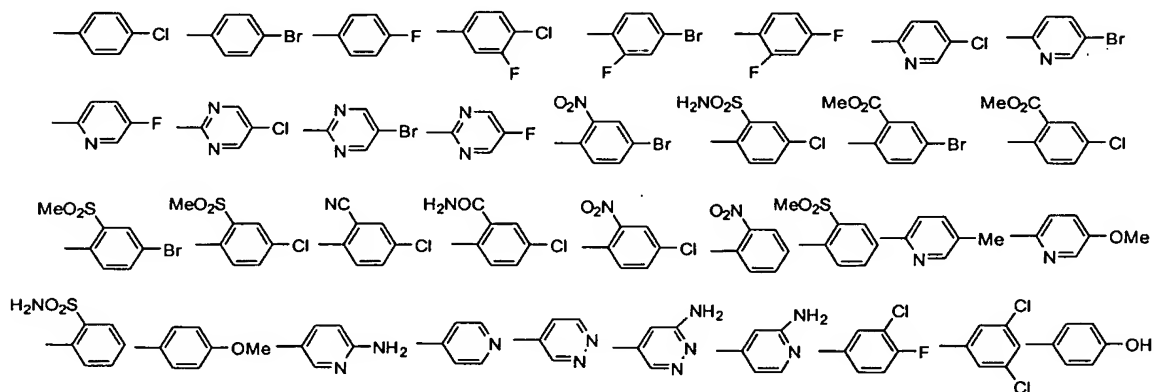
H; C_{1-4} -alkyl and $-C_{0-4}$ -alkyl-carbocyclic aryl;

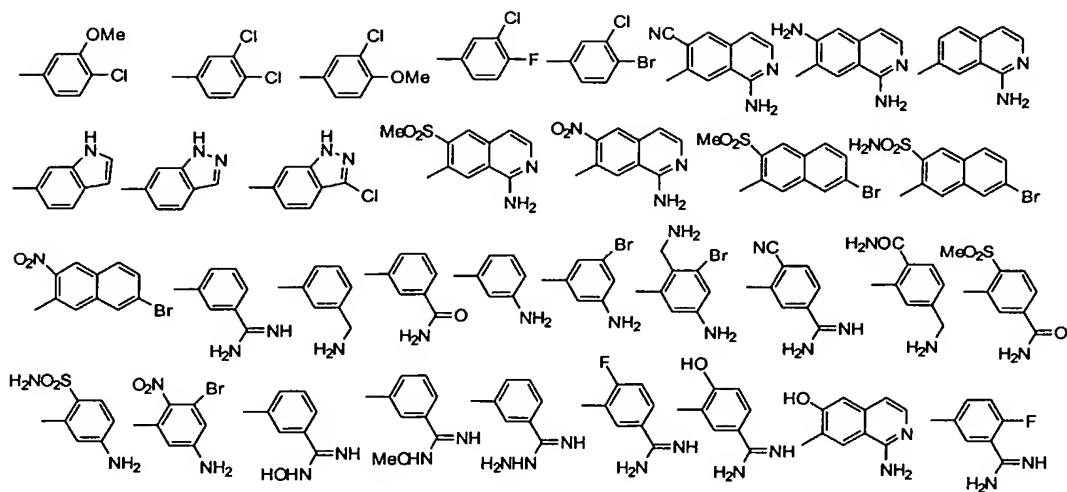
- 20 and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.



J is a member selected from the group consisting of:
a direct link, -O-, -NH-, -C(=O)-NH- and -NH-C(=O)-;

5 X is a member selected from the group consisting of:

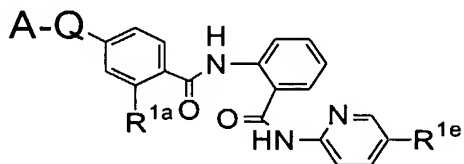




and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

5

4. A compound of claim 1, having the following structure:



wherein:

R^{1a} is a member selected from the group consisting of:

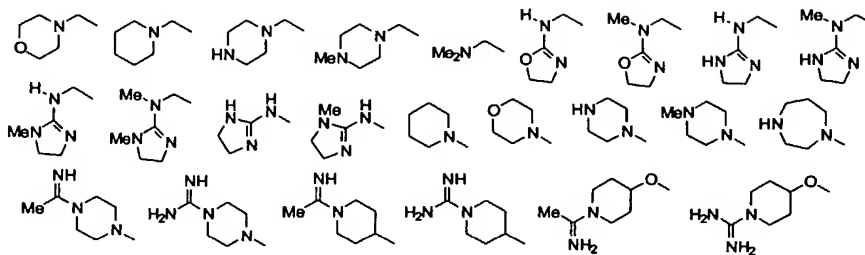
10

H, -F, -Cl and -Br;

R^{1e} is a member selected from the group consisting of:

H, -F, -Cl, -Br, -OMe, -OH, -Me, -CF₃ and -CH₂NH₂; and

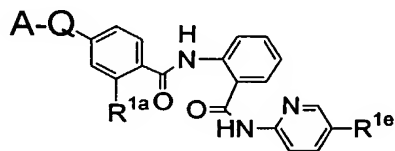
A-Q is a member selected from the group consisting of:



and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

5

6. A compound of claim 1 having the following structure:



wherein:

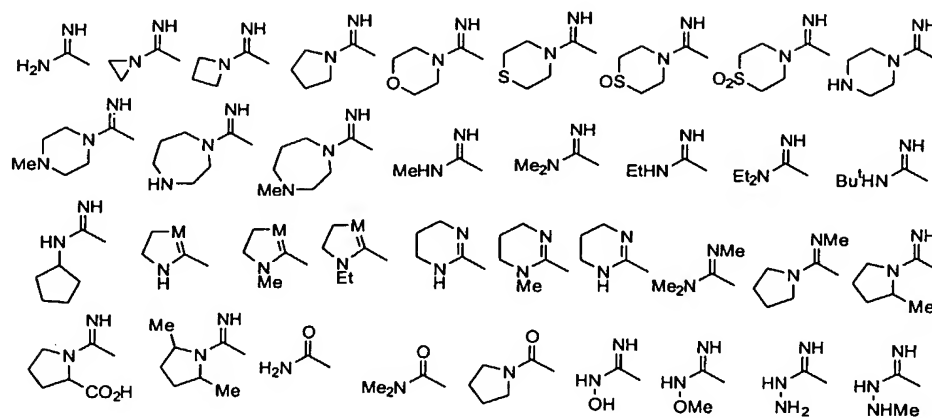
10 R^{1a} is a member selected from the group consisting of:

H, -F, -Cl and -Br;

R^{1e} is a member selected from the group consisting of:

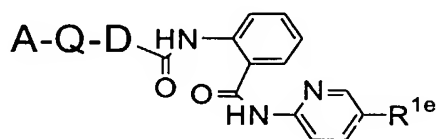
H, -F, -Cl, -Br, -OMe, -OH, -Me, -CF₃ and -CH₂NH₂;

A-Q is a member selected from the group consisting of:



5 and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

7. A compound of claim 1 having the following structure:

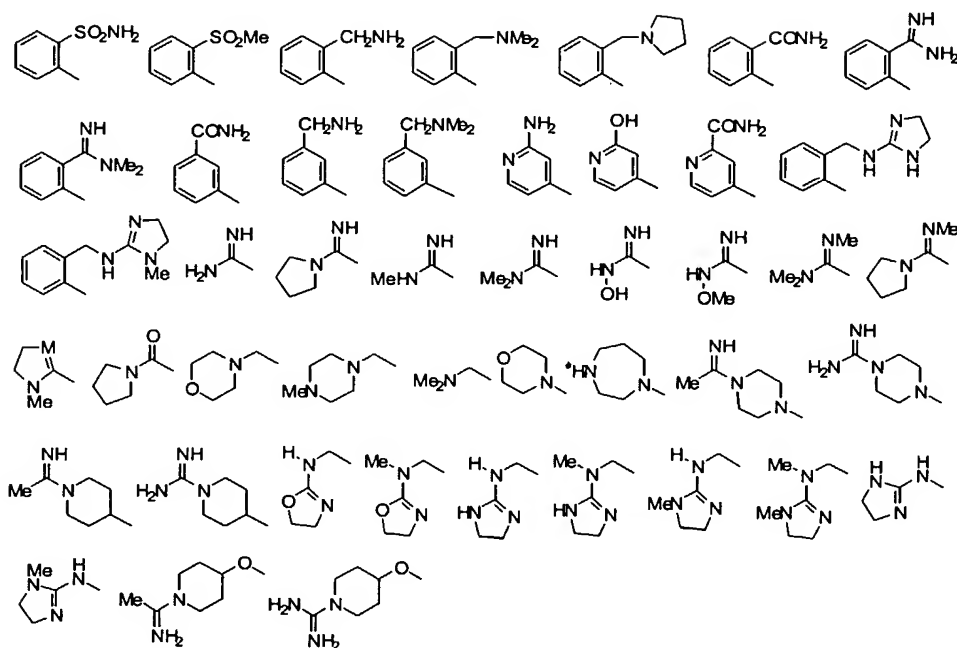


wherein:

10 R^{1e} is a member selected from the group consisting of:

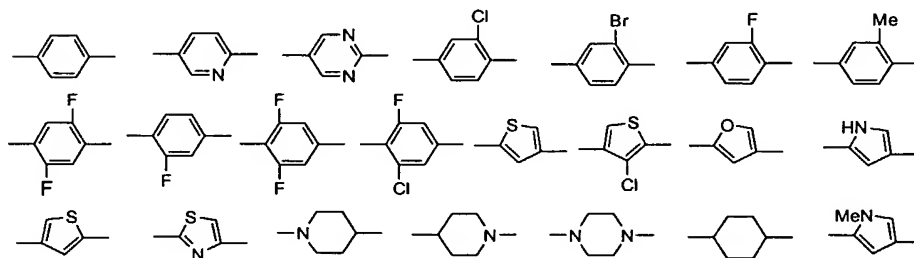
H, -F, -Cl, -Br, -OMe, -OH, -Me, -CF₃ and -CH₂NH₂;

A-Q is a member selected from the group consisting of:



D is a member selected from the group consisting of:

5



and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

10 8. A compound of claim 1 having the following structure:

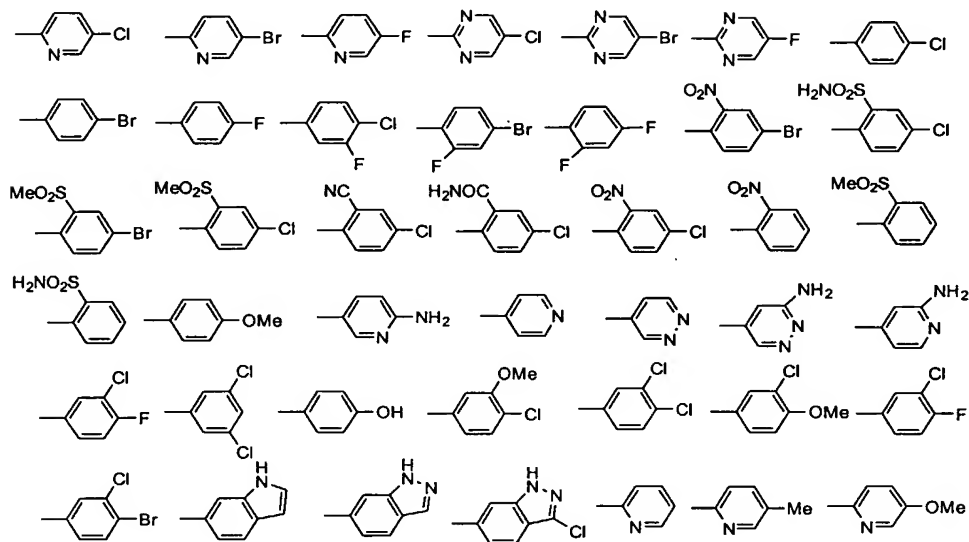


wherein:

J is a member selected from the group consisting of:

5 -NHC(=O)-, -C(=O)NH-;

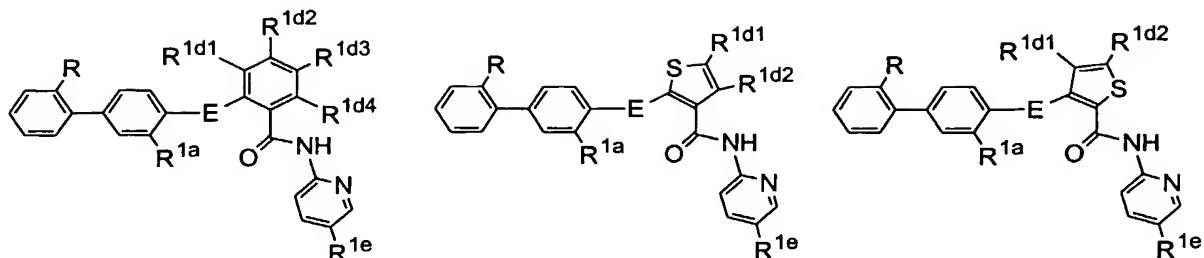
X is a member selected from the group consisting of:



10 and all pharmaceutically acceptable isomers, salts, hydrates, solvates and
prodrug derivatives thereof.

9. A compound of claim 1 having the following structure:

191



wherein:

R is a member selected from the group of :

-SO₂-NH₂ and -SO₂Me;

5

R^{1a} is a member selected from the group of:

H, -F, -Cl and Br;

E is a member selected from the group consisting of:

10

-NHC(=O)- and -C(=O)NH-;

R^{1d1}, R^{1d2}, and R^{1d4} are independently a member selected from the group of:

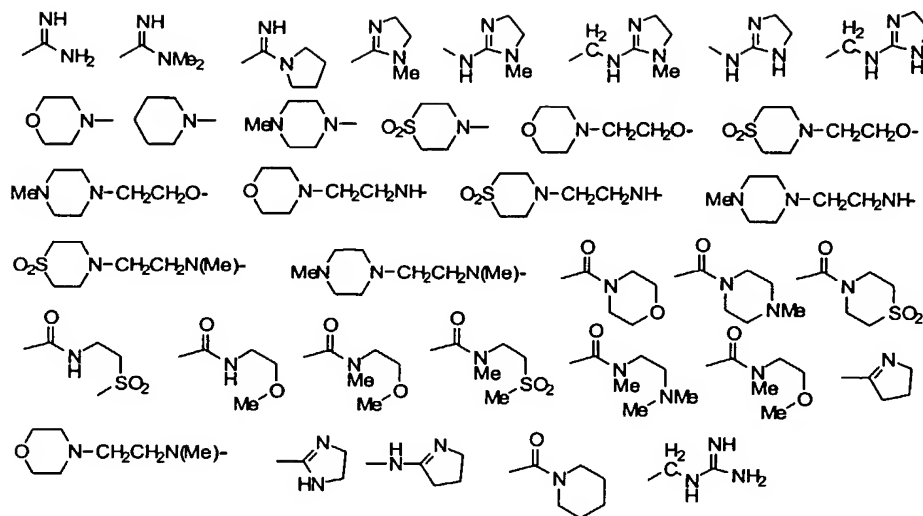
H, -F, -Cl, -Br, -Me, -NO₂, -OH, -OMe, -NH₂, -NHAc, -NHSO₂Me, -CH₂OH
and -CH₂NH₂;

15

R^{1d3} is a member selected from the group of:

H, -CH₃, -CF₃, -Cl, -F, -Br, -NH₂, -N(-Me)₂, -OH, -OMe, -NHSO₂Me, -NO₂,
-CN, -C(=O)-OMe, -CO₂H, -C(=O)-NH₂, -SO₂NH₂, -SO₂CH₃, -NHC(=O)-Me,
-C(=O)-N(-Me)₂, -CH₂NH₂, -CH₂-N(-Me)₂, -CH₂OH, -OCH₂CO₂H,
-OCH₂C(=O)-OMe, -OCH₂C(=O)-NH₂, and -OCH₂C(=O)-N(-Me)₂,

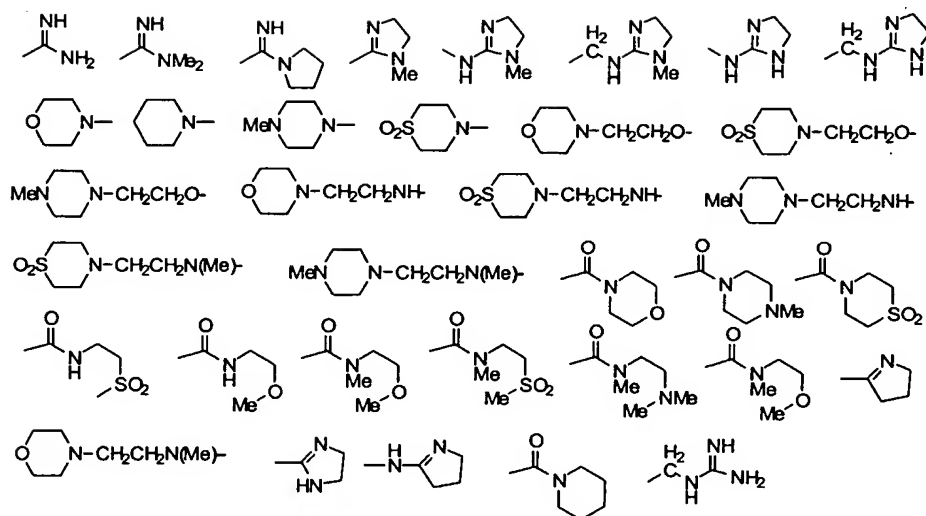
20



R^{1c} is a member selected from the group of :

F, -Cl, -Br, -OH, -Me and -Ome,

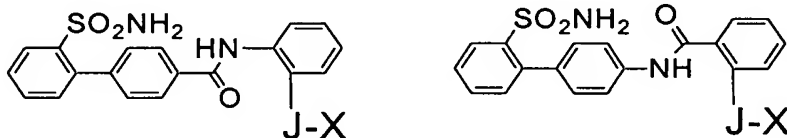
and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.



and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

5

11. A compound of claim 1 having the following structure:



10 wherein:

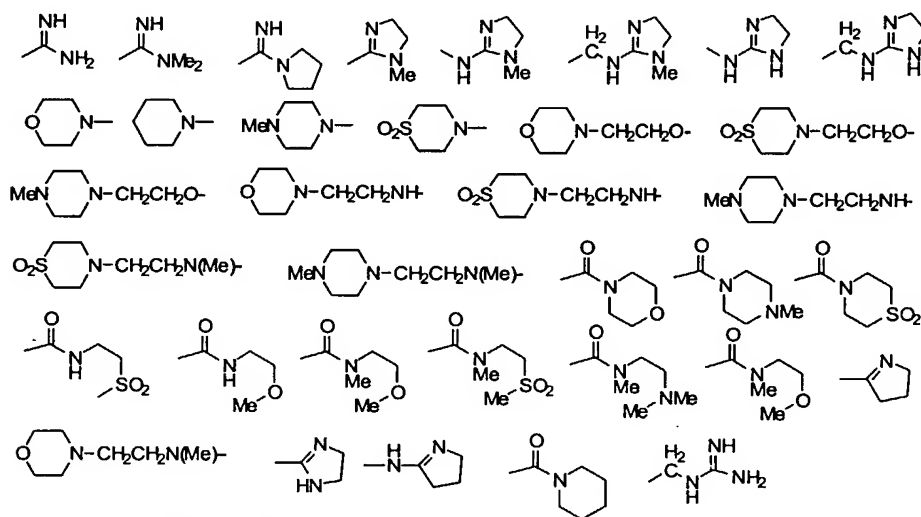
-NHC(=O)- and -C(=O)NH-, O;

R^{1d1} , R^{1d2} , and R^{1d4} are independently a member selected from the group of:

H, -F, -Cl, -Br, -Me, -NO₂, -OH, -OMe, -NH₂, -NHAc, -NHSO₂Me, -CH₂OH, -CH₂NH₂:

R^{Id3} is a member selected from the group of:

H, -CH₃, -CF₃, -Cl, -F, -Br, -NH₂, -N(-Me)₂, -OH, -OMe, -NHSO₂Me, -NO₂, -CN, -CO₂Me, -CO₂H, -C(=O)-NH₂, -SO₂NH₂, -SO₂CH₃, -NHC(=O)-Me, -C(=O)-N(-Me)₂, -CH₂NH₂, -CH₂-N(-Me)₂, -CH₂OH, -OCH₂CO₂H, -OCH₂C(=O)-OMe, -OCH₂C(=O)-NH₂, -OCH₂C(=O)-N(-Me)₂.

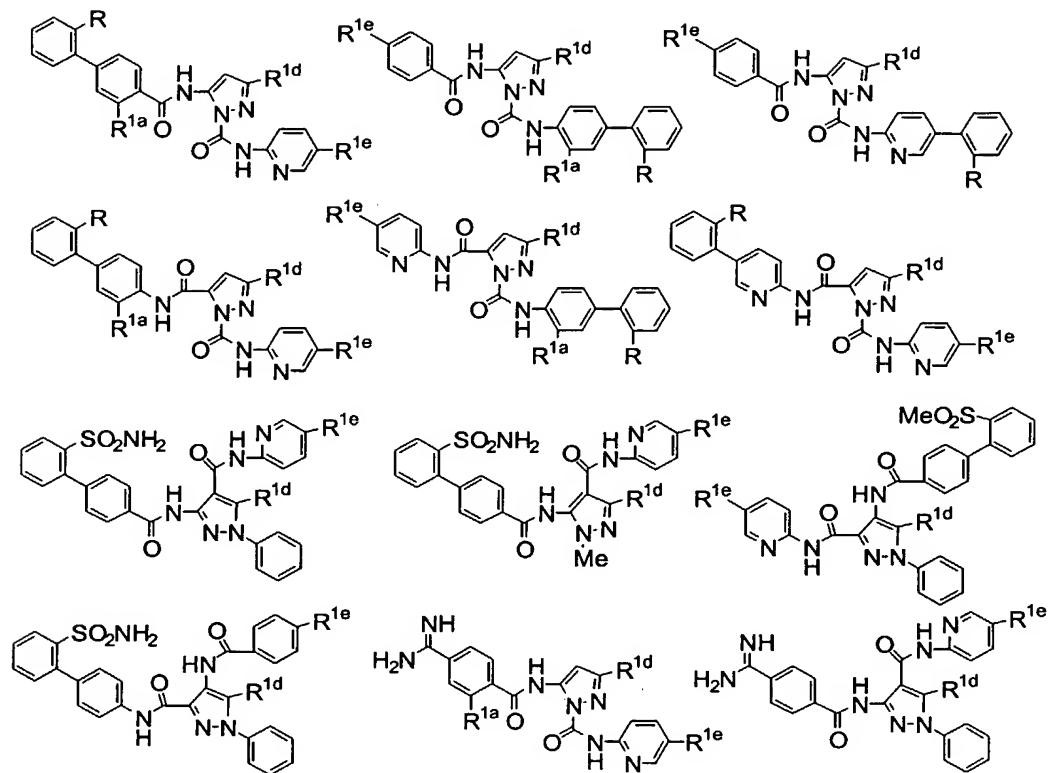


R^{1e} is a member selected from the group of :

F, -Cl, -Br, -OH, -Me and -OMe;

15 and all pharmaceutically acceptable isomers, salts, hydrates, solvates and
prodrug derivatives thereof.

13. A compound of claim 1 selected from the group consisting of:



5

wherein:

R is a member selected from the group of:

-SO₂-NH₂, and -SO₂Me;

10

R^{1a} is a member selected from the group of:

H, -F, -Cl and Br;

R^{1d} is a member selected from the group consisting of:

-H, -CH₃, -CF₃, -CN, -SO₂NH₂ and -SO₂CH₃; and

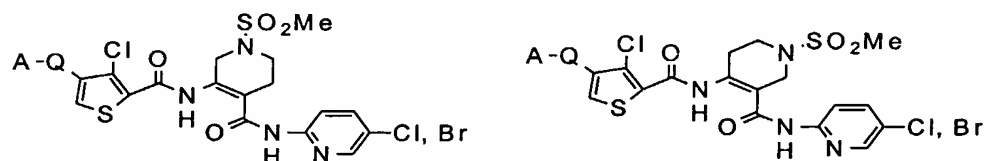
15

R^{1e} is a member selected from the group of:

-Cl and -Br;

and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

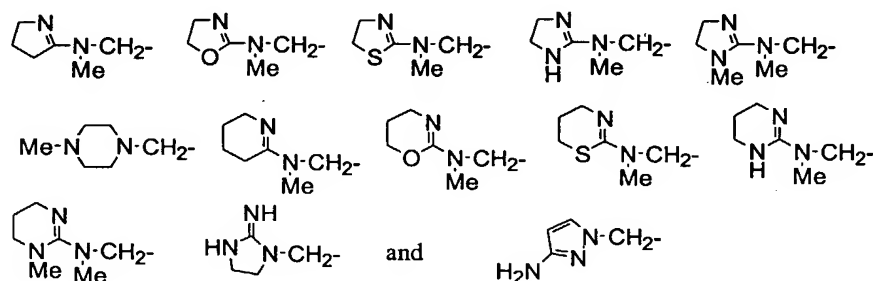
- 5 14. A compound of claim 1 having the following structure:



wherein:

10

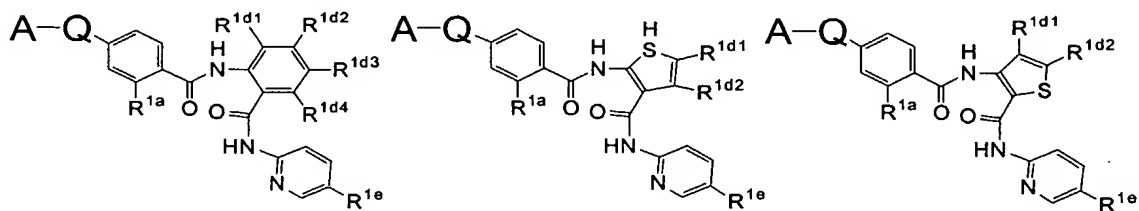
A-Q taken together are a member selected from the group consisting of:



and all pharmaceutically acceptable isomers, salts, hydrates, solvates and

15 prodrug derivatives thereof.

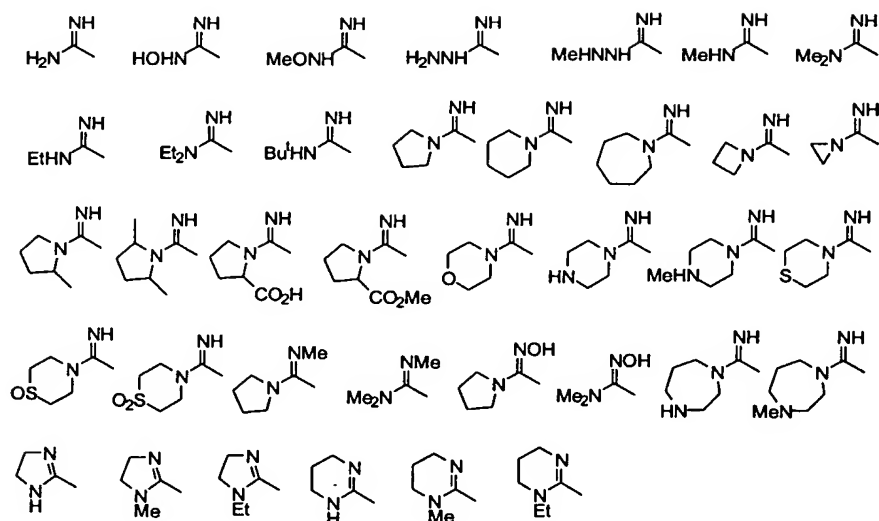
15. A compound of claim 1 selected from the group consisting of:



wherein:

A-Q is a member selected from the group of :

5



R^{1a} is a member selected from the group of:

H, -F, -Cl and Br;

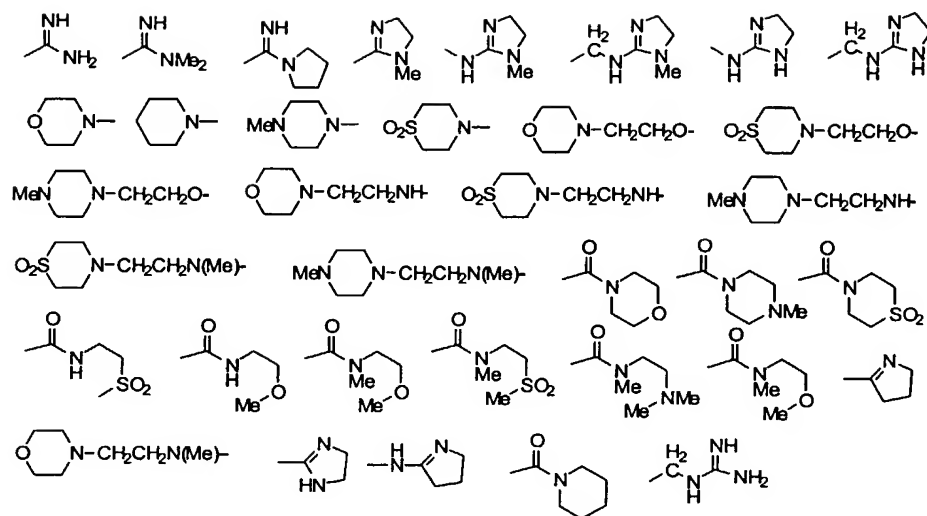
10

R^{1d1}, R^{1d2}, and R^{1d4} are independently a member selected from the group of:

H, -F, -Cl, -Br, -Me, -NO₂, -OH, -OMe, -NH₂, -NHAc, -NHSO₂Me, -CH₂OH, -CH₂NH₂

15 R^{1d3} is a member selected from the group of:

H, -CH₃, -CF₃, -Cl, -F, -Br, -NH₂, -N(-Me)₂, -OH, -OMe, -NHSO₂Me, -NO₂, -CN, -C(=O)-OMe, -CO₂H, -C(=O)-NH₂, -SO₂NH₂, -SO₂CH₃, -NHC(=O)-Me, -C(=O)-N(Me)₂, -CH₂NH₂, -CH₂-N(-Me)₂, -CH₂OH, -OCH₂CO₂H, -OCH₂C(=O)-OMe, -OCH₂C(=O)-NH₂, -OCH₂C(=O)-N(-Me)₂.



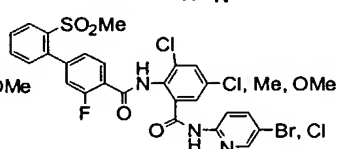
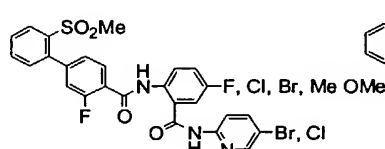
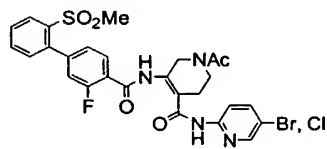
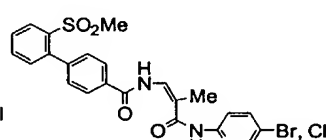
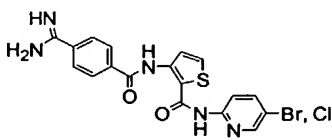
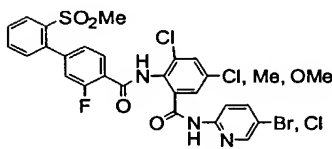
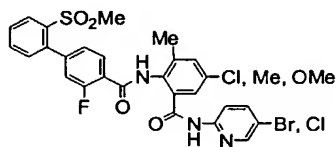
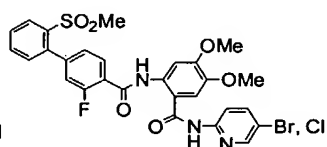
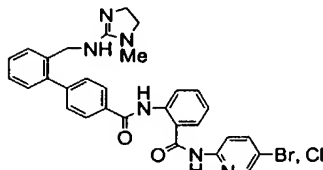
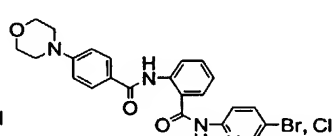
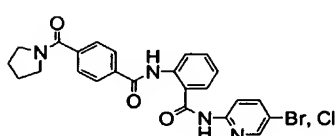
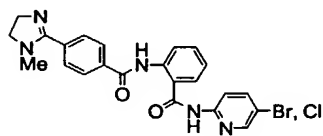
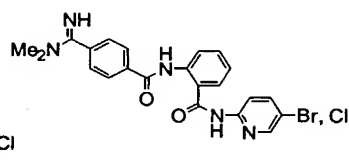
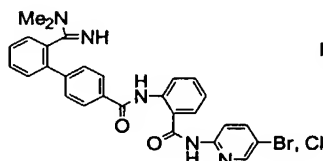
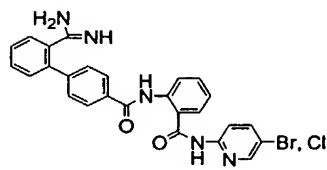
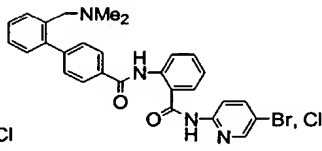
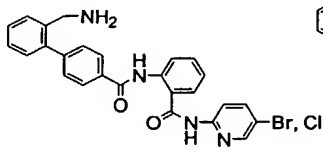
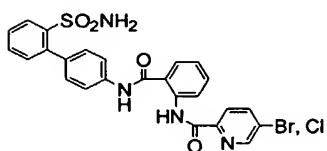
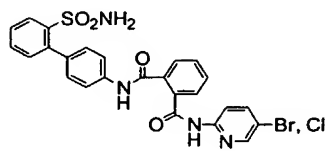
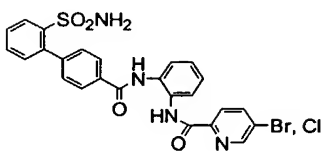
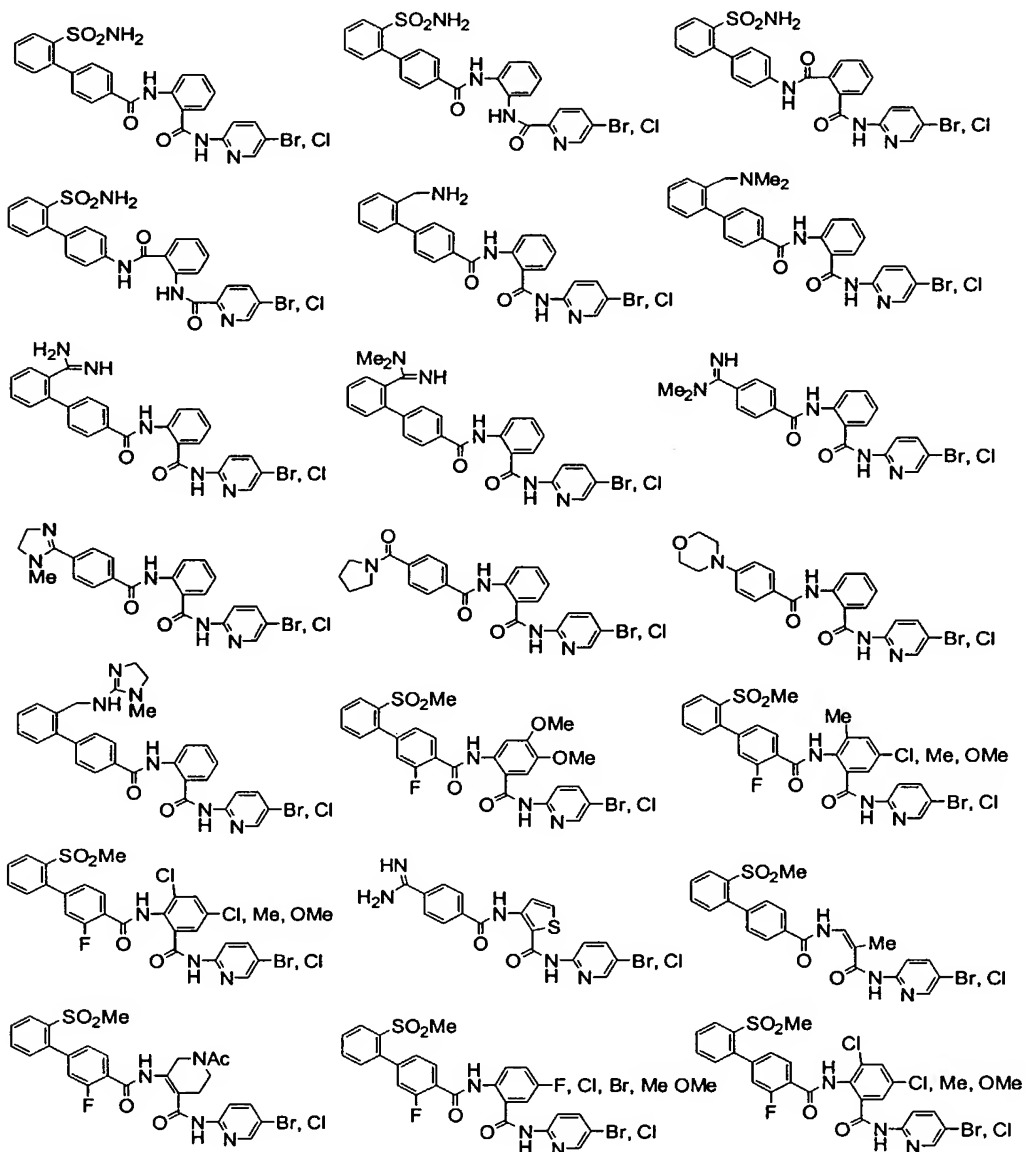
R^{1e} is a member selected from the group of:

F, -Cl, -Br, -OH, -Me and -OMe;

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and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

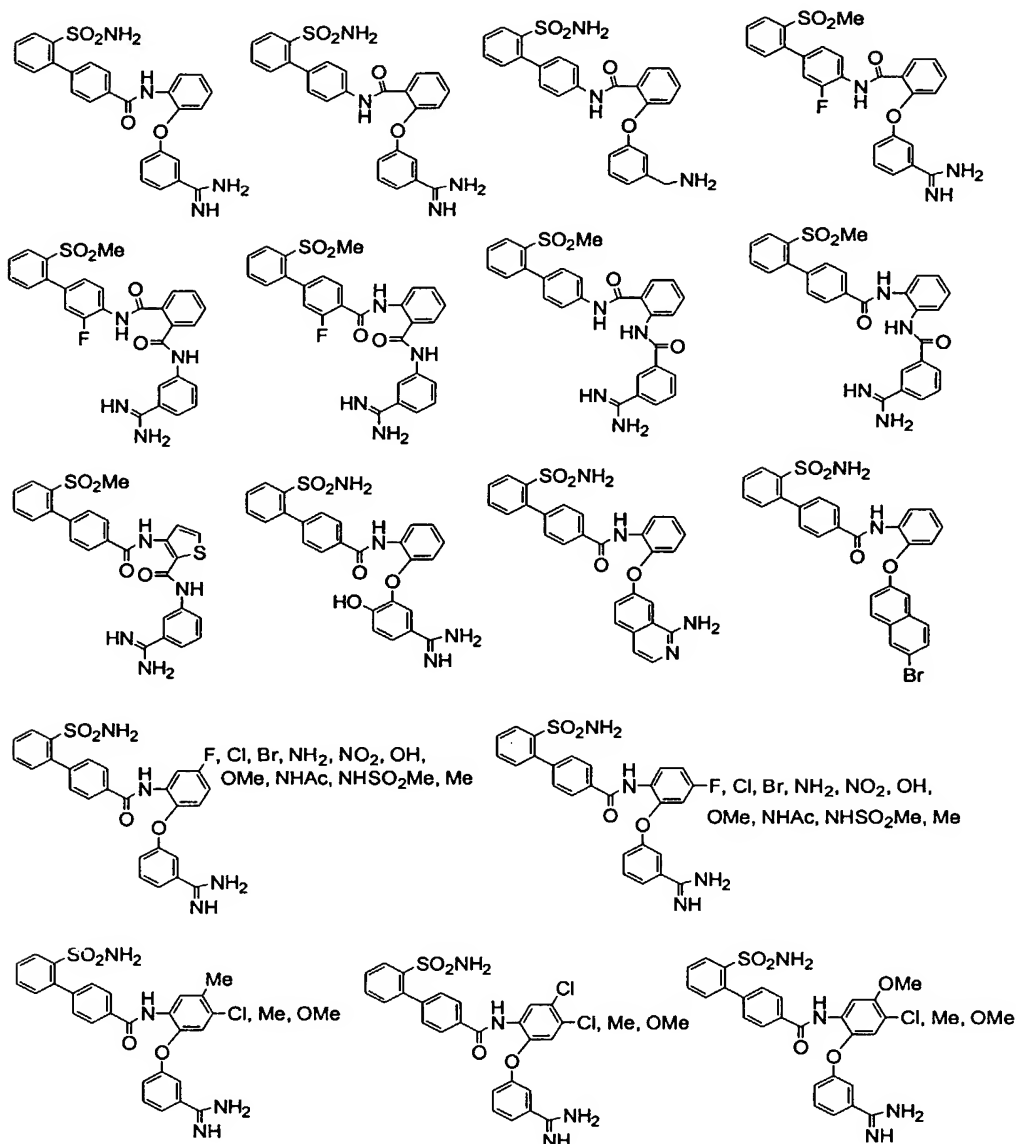
16. A compound of claim 1 selected from the group of consisting of:



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and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

17. A compound of claim 1 selected from the group consisting of:



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and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

18. A compound of claim 1 selected from the group consisting of:

- 3-(2-(4-[(2-aminosulfonyl)phenyl]benzoylamino) phenoxy)benzamidine, 3-(4-fluoro-2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)phenoxy) benzamidine, 3-(4-trifluoromethyl-2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)phenoxy)
- 5 benzamidine, 3-(4-methylsulfonyl-2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)phenoxy) benzamidine, 3-(5-hydroxy-2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)phenoxy) benzamidine, 3-(4-methoxycarbonyl-2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)phenoxy) benzamidine, 3-(4-hydroxycarbonyl-2-(4-[(2-
- 10 aminosulfonyl)phenyl]phenylcarbonylamino)phenoxy) benzamidine, 3-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)pheylamino) benzamidine, 7-(2-(4-[(2-aminosulfonyl)phenyl]benzoylamino)phenoxy)-1-aminoisoquinoline, 7-(2-(4-[(2-aminosulfonyl)phenyl]benzoylamino)-4-fluorophenoxy)1-aminoisoquinoline, 7-(2-(4-[(2-aminosulfonyl)phenyl]benzoylamino)-4-trifluoromethylphenoxy)1-
- 15 aminoisoquinoline, 7-(2-(4-[(2-aminosulfonyl)phenyl]benzoylamino)-4-methylsulfonylphenoxy)1-aminoisoquinoline, 3-(2-(4-[(2-aminosulfonyl)phenyl]phenylaminocarbonyl-4-nitrophenoxy) benzamidine, 3-(2-(4-[(2-aminosulfonyl)phenyl]phenylaminocarbonyl-4-aminophenoxy) benzamidine, 3-(2-(4-[(2-aminosulfonyl)phenyl]phenylaminocarbonyl-4-chlorophenoxy)
- 20 benzamidine, 3-(2-(4-[(2-aminosulfonyl)phenyl]phenylaminocarbonyl-4-bromophenoxy) benzamidine, 2-bromo-6-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)phenoxy) naphthalene, 3-methoxycarbonyl-2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)phenoxy naphthalene, 3-hydroxycarbonyl-2-(4-[(2-
- 25 aminosulfonyl)phenyl]phenylcarbonylamino)phenoxy naphthalene, 3-aminocarbonyl-2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)phenoxy naphthalene, 3-methoxycarbonyl-2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)phenoxy-6-bromo naphthalene, 3-hydroxycarbonyl-2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)phenoxy-6-bromo naphthalene, N-(5-bromo-2-pyridinyl)-(2-(4-[(2-
- 30 aminosulfonyl)phenyl]phenylcarbonylamino)phenylcarboxamide, N-(5-chloro-2-pyridinyl)-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)phenylcarboxamide, N-(5-bromo-2-pyridinyl)-(2-(4-[(2-methylsulfonyl)phenyl]phenylcarbonyl)amino)phenylcarboxamide,

- N-(5-chloro-2-pyridinyl)-(2-(4-[(2-methylsulfonyl)phenyl]phenylcarbonyl)amino)phenylcarboxamide, N-(4-bromo-2-methoxycarbonylphenyl)-(2-(4-[(2-methylsulfonyl)phenyl]phenylcarbonyl)amino)phenylcarboxamide, N-(4-chloro-2-methoxycarbonylphenyl)-(2-(4-[(2-methylsulfonyl)phenyl]phenylcarbonyl)amino)phenylcarboxamide, N-(5-bromo-2-pyridinyl)-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonyl)amino)pyridinyl-3-carboxamide,
- 5 N-(5-chloro-2-pyridinyl)-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonyl)amino)pyridinyl-3-carboxamide, N-(5-bromo-2-pyridinyl)-(3-(4-[(2-aminosulfonyl)phenyl]phenylcarbonyl)amino)pyridinyl-2-carboxamide, N-(5-chloro-2-pyridinyl)-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonyl)amino)pyridinyl-3-carboxamide, N-(4-bromo-2-nitrophenyl)-(2-(4-[(2-methylsulfonyl)phenyl]phenylcarbonyl)amino)phenylcarboxamide, N-(4-bromophenyl)-N'-(4-[(2-aminosulfonyl)phenyl]phenyl)-maleamic amide, N¹-(5-bromopyridin-2-yl)-N⁴-(4-[(2-aminosulfonyl)phenyl]phenyl)-2-methylmaleamic amide, N¹-(5-bromopyridin-2-yl)-N⁴-(4-[(2-aminosulfonyl)phenyl]phenyl)-3-methylmaleamic amide, N-(5-bromo-2-pyridinyl)-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonyl)amino)-4-nitrophenylcarboxamide, N-(5-bromo-2-pyridinyl)-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonyl)amino)-4-aminophenylcarboxamide, N-(5-chloro-2-pyridinyl)-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonyl)amino)-4-aminophenylcarboxamide, N-(5-bromo-2-pyridinyl)-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonyl)amino)-4-methylsulfonylaminophenylcarboxamide, N-(5-chloro-2-pyridinyl)-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonyl)amino)-4-methylsulfonylaminophenylcarboxamide, N-(5-bromo-2-pyridinyl)-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonyl)amino)-5-aminophenylcarboxamide, N-(5-chloro-2-pyridinyl)-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonyl)amino)-5-aminophenylcarboxamide, N-(5-bromo-2-pyridinyl)-(2-(4-amidinophenylcarbonyl)amino)-phenylcarboxamide, N-(5-bromo-2-pyridinyl)-(2-(4-(2-imidazolyl)phenylcarbonyl)amino)-phenylcarboxamide, N-(5-bromo-2-pyridinyl)-(2-(4-(5-tetrazolyl)phenylcarbonyl)amino)-phenylcarboxamide, N-(5-bromo-2-pyridinyl)-(2-(4-[1,1-doxo(1,4-thiazaperhydroin-4-yl)]iminimethyl)phenylcarbonyl)amino)-phenylcarboxamide, N-(5-bromo-2-
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- 15
- 20
- 25
- 30
- 35

- pyridinyl)-(2-(4-[1-oxo(1,4-thiazaperhydroin-4-yl))iminomethyl]phenylcarbonyl)amino)-phenylcarboxamide, N-(5-bromo-2-pyridinyl)-(2-4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)-4,5-difluorophenylcarboxamide, 3-(2-(4-[(2-aminosulfonyl)phenyl]-2-fluorophenylaminocarbonyl-4-aminophenoxy) benzamidine, 3-(2-(4-[(2-aminosulfonyl)phenyl]-2-fluorophenylaminocarbonyl-4-aminophenoxy) benzamidine, 3-(2-(4-[(2-aminosulfonyl)phenyl]benzoylamino) phenoxy)benzylamine, 2-[4-(N-{2-[N-(5-chloro-2-pyridyl)carbamoyl]phenyl}carbamoyl)phenyl]-benzenecarboxamidine, (4-{2-[(dimethylamino)iminomethyl]phenyl}phenyl)-N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl}carboxamide, N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl} {4-[2-((hydroxyamino)iminomethyl)-phenyl]phenyl}carboxamide, 2-[4-(N-{2-[N-(5-chloro-2-pyridyl)carbamoyl]phenyl}carbamoyl)phenyl]benzamide, {4-[2-(aminomethyl)phenyl]phenyl}-N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl}carboxamide, [4-(aminomethyl)phenyl]-N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl}carboxamide, N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl} {4-[(2-imidazolin-2-ylamino)methyl]phenyl}carboxamide, N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl} {4-[(1-methyl(2-imidazolin-2-yl))amino]methyl}phenyl}carboxamide, N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)} {4-(1-methyl(2-imidazolin-2-yl))phenyl}carboxamide, {4-[(dimethylamino)iminomethyl]phenyl}-N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)}carboxamide, 4-(N-{2-[N-(5-chloro-2-pyridyl)carbamoyl]-3-thienyl}carbamoyl)benzenecarboxamidine, N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)} {4-(iminopiperidylmethyl)-phenyl}carboxamide, N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)} {4-(iminopyrrolidinylmethyl)-phenyl}carboxamide, N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)} {4-(iminomorpholin-4-ylmethyl)phenyl}carboxamide, N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)} {4-(imino-1,4-thiazaperhydroin-4-ylmethyl)phenyl}carboxamide, [4-(azaperhydroepinyliminomethyl)phenyl]-N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)}carboxamide, N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)} {4-[imino(2-methylpyrrolidinyl)methyl]phenyl}carboxamide, N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)} {4-[imino(methylamino)methyl]phenyl}carboxamide, N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)} {4-(3-methyl(3,4,5,6-tetrahydropyrimidin-2-yl))phenyl}carboxamide, N-{2-[N-(5-chloro(2-

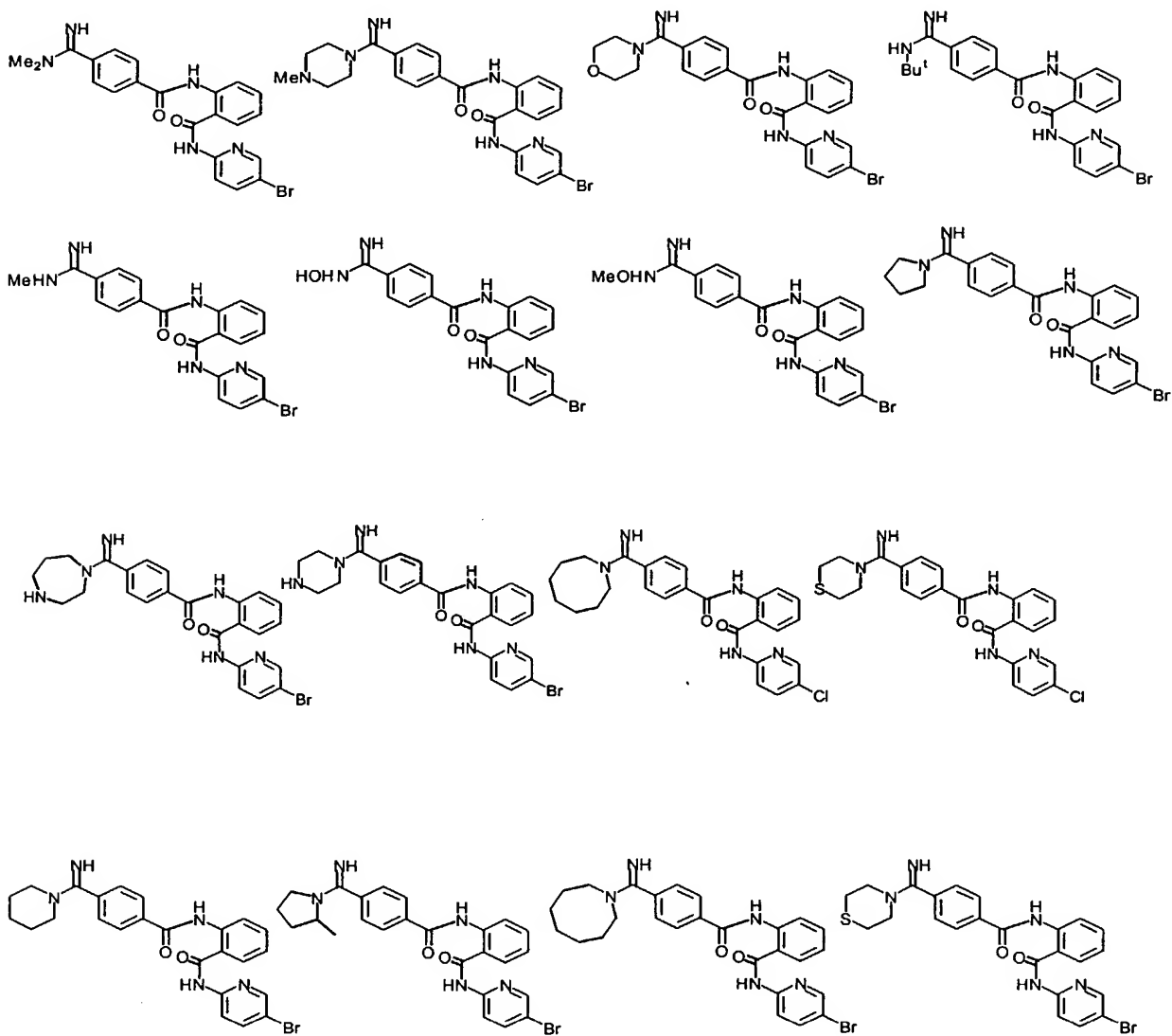
- pyridyl))carbamoyl](3-thienyl))[4-((hydroxyamino)iminomethyl)-phenyl]carboxamide, 1- {[4-(N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl))carbamoyl]phenyl}-iminomethyl}pyrrolidine-2-carboxylic acid, N-{2-[N-(5-bromo(2-pyridyl))carbamoyl](3-thienyl))[4-(1-methyl(2-imidazolin-2-yl))phenyl]carboxamide, 4-(N-{2-[N-(5-bromo(2-pyridyl))carbamoyl]-3-thienyl}carbamoyl)benzenecarboxamidine, N-{2-[N-(5-bromo(2-pyridyl))carbamoyl](3-thienyl))[4-(iminopyrrolidinylmethyl)phenyl]carboxamide, N-{2-[N-(5-bromo(2-pyridyl))carbamoyl](3-thienyl))[4-(iminopiperidylmethyl)phenyl]carboxamide, N-{2-[N-(5-bromo(2-pyridyl))carbamoyl](3-thienyl))[4-(iminomorpholin-4-ylmethyl)phenyl]carboxamide, N-{2-[N-(5-bromo(2-pyridyl))carbamoyl](3-thienyl))[4-(imino-1,4-thiazaperhydroin-4-ylmethyl)phenyl]carboxamide, N-{3-[N-(5-chloro(2-pyridyl))carbamoyl](2-thienyl))[4-(iminopyrrolidinylmethyl)phenyl]carboxamide, N-{3-[N-(5-chloro(2-pyridyl))carbamoyl](2-thienyl))[4-(1-methyl(2-imidazolin-2-yl))phenyl]carboxamide, 3-[(3-{[4-(2-sulfamoylphenyl)phenyl]carbonylamino}-2-thienyl)carbonylamino]benzenecarboxamidine, N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl))[4-(2-sulfamoylphenyl)phenyl]carboxamide, N-{2-[N-(5-bromo(2-pyridyl))carbamoyl](3-thienyl))[4-(2-sulfamoylphenyl)phenyl]carboxamide, N-(5-bromo-2-pyridinyl)-(2-4-[(2-aminosulfonyl)phenyl]phenylaminocarbonyl)5-methyl-pyrazolcarboxamide, N-(5-bromo-2-pyridinyl)-(2-4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)-5-fluorophenylcarboxamide, N-(5-bromo-2-pyridinyl)-(2-4-[(2-aminosulfonyl)phenyl]phenylaminocarbonylamino)-5-fluorophenylcarboxamide, N-(5-bromo-2-pyridinyl)-(2-(4-amidinophenylcarbonyl)amino)5-fluorophenylcarboxamide, N-(5-bromo-2-pyridinyl)-(2-(4-(1-methyl-2-imadazolin-2-yl)phenylcarbonyl)amino)5-fluorophenylcarboxamide, N-{2-[N-(5-bromo(2-pyridyl))carbamoyl]-4,5-dimethoxyphenyl}(4-cyanophenyl)carboxamide, (4,5-dimethoxy-2-{[4-(1-methyl(2-imidazolin-2-yl))phenyl]carbonylamino}phenyl)-N-(5-bromo(2-pyridyl))carboxamide, 4-(N-{2-[N-(5-bromo(2-pyridyl))carbamoyl]-4,5-dimethoxyphenyl}carbamoyl)-benzenecarboxamidine, N-(5-chloro(2-pyridyl)){2-[(4-cyanophenyl)carbonylamino]-5-methoxyphenyl}-carboxamide, N-(5-chloro(2-pyridyl))(5-methoxy-2-{[4-(1-methyl(2-imidazolin-2-yl))phenyl]carbonylamino}phenyl)carboxamide, 4-(N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]-4-methoxyphenyl}carbamoyl)benzene-carboxamidine, N-(5-chloro(2-pyridyl))[2-({4-imino(methylamino)methyl}phenyl)carbonylamino)-5-methoxyphenyl]carboxamide,

- [2-({4-[(dimethylamino)iminomethyl]phenyl} carbonylamino)-5-methoxyphenyl]-N-(5-chloro(2-pyridyl))carboxamide, N-(5-chloro(2-pyridyl))(2-{[4-(iminopyrrolidinylmethyl)phenyl]carbonylamino}-5-methoxyphenyl)carboxamide, N-(5-chloro(2-pyridyl))(2-{[4-(iminopiperidylmethyl)phenyl]carbonylamino}-5-methoxyphenyl)carboxamide, N-(5-chloro(2-pyridyl))(2-{[4-(iminomorpholin-4-ylmethyl)phenyl]carbonylamino}-5-methoxyphenyl)carboxamide, N-(5-chloro(2-pyridyl))(2-{[4-(imino-1,4-thiazaperhydroin-4-ylmethyl)phenyl]carbonylamino}-5-methoxyphenyl)carboxamide, (2-{[4-(amino(hydroxyimino)methyl)phenyl]carbonylamino}-5-methoxyphenyl)-N-(5-chloro(2-pyridyl))carboxamide, N-(5-bromo(2-pyridyl))(2-{[4-(cyanophenyl)carbonylamino]-5-methoxyphenyl} carboxamide, N-(5-bromo(2-pyridyl))(5-methoxy-2-{[4-(1-methyl(2-imidazolin-2-yl))phenyl]carbonylamino} phenyl)carboxamide, 4-(N-{2-[N-(5-bromo(2-pyridyl))carbamoyl]-4-methoxyphenyl} carbamoyl)benzenecarboxamidine, N-(5-bromo(2-pyridyl))[2-({4-[imino(methylamino)methyl]phenyl} carbonylamino)-5-methoxyphenyl]carboxamide, [2-({4-[(dimethylamino)iminomethyl]phenyl} carbonylamino)-5-methoxyphenyl]-N-(5-bromo(2-pyridyl))carboxamide, N-(5-chloro(2-pyridyl))(2-{[4-(iminopyrrolidinylmethyl)phenyl]carbonylamino}-5-methoxyphenyl)carboxamide, N-(5-bromo(2-pyridyl))(2-{[4-(iminopiperidylmethyl)phenyl]carbonylamino}-5-methoxyphenyl)carboxamide, N-(5-bromo(2-pyridyl))(2-{[4-(iminomorpholin-4-ylmethyl)phenyl]carbonylamino}-5-methoxyphenyl)carboxamide, N-(5-bromo(2-pyridyl))(2-{[4-(imino-1,4-thiazaperhydroin-4-ylmethyl)phenyl]carbonylamino}-5-methoxyphenyl)carboxamide, (2-{[4-(amino(hydroxyimino)methyl)phenyl]carbonylamino}-5-methoxyphenyl)-N-(5-bromo(2-pyridyl))carboxamide, N-(5-chloro(2-pyridyl)){6-[4-(cyanophenyl)carbonylamino]-3-hydroxyphenyl} carboxamide, ethyl 2-{3-[N-(5-chloro(2-pyridyl))carbamoyl]-4-[(4-cyanophenyl)carbonylamino]-phenoxy} acetate, methyl 2-[4-({4-[(dimethylamino)iminomethyl]phenyl} carbonylamino)-3-[N-(5-chloro(2-pyridyl))carbamoyl]phenoxy} acetate, (6-{[4-(amino(hydroxyimino)methyl)phenyl]carbonylamino}-3-hydroxyphenyl)-N-(5-chloro(2-pyridyl))carboxamide, 4-(N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]-4-hydroxyphenyl} carbamoyl)-benzenecarboxamidine, and 4-(N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]-4-hydroxyphenyl} carbamoyl)-benzenecarboxamidine,

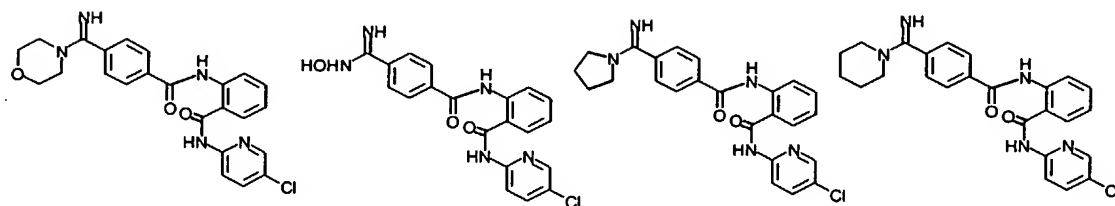
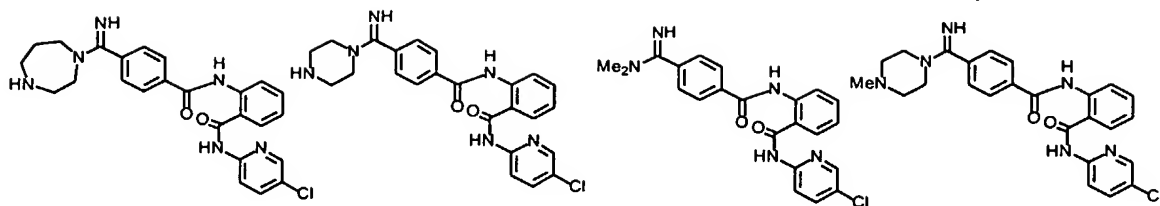
and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

19. The compound according to claim 1 selected from the group consisting of:

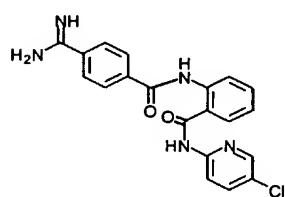
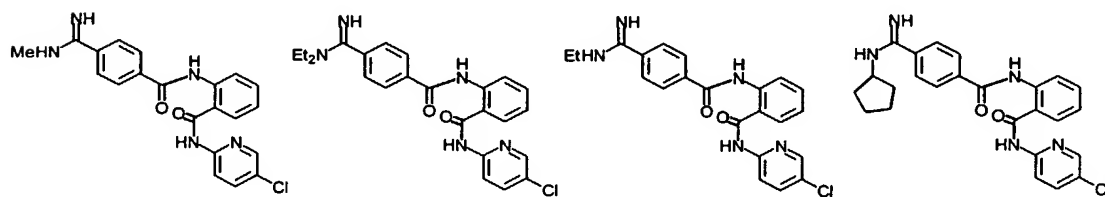
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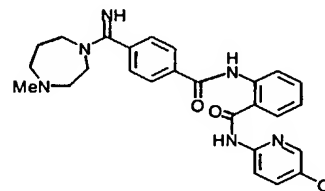
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and

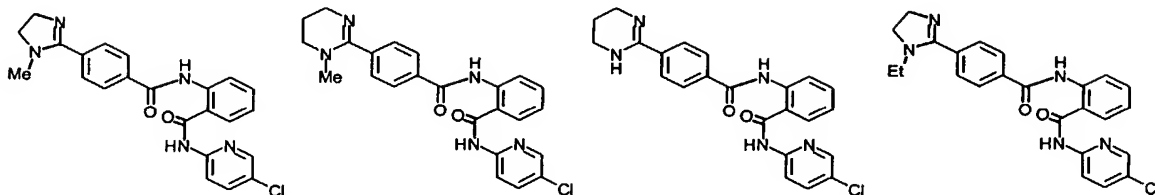


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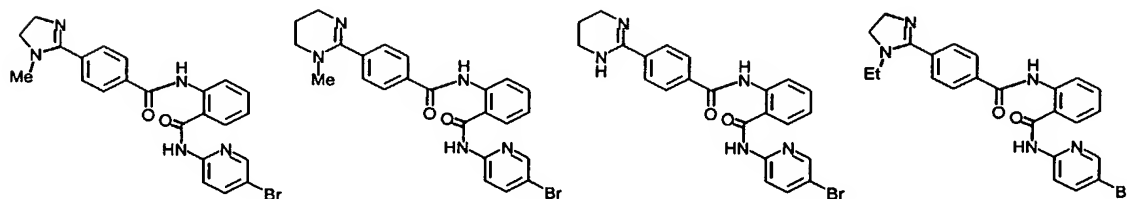
and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

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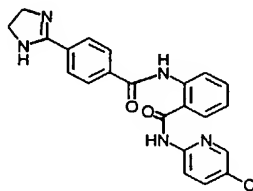
20. The compound according to claim 1 selected from the group consisting of:



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and



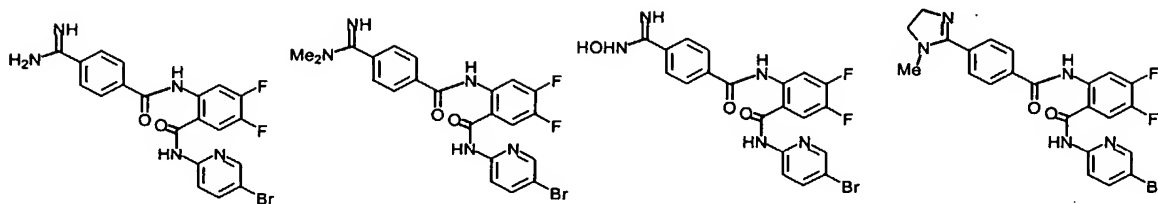
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and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

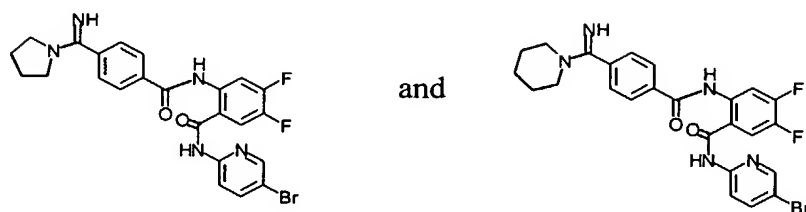
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21. The compound according to claim 1 selected from the group consisting of:



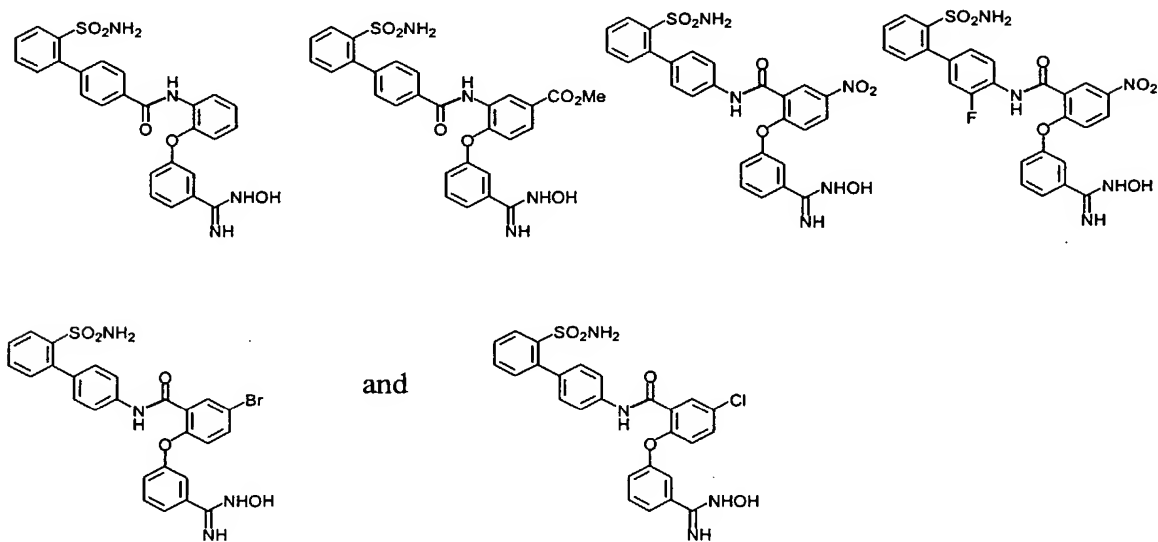
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and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

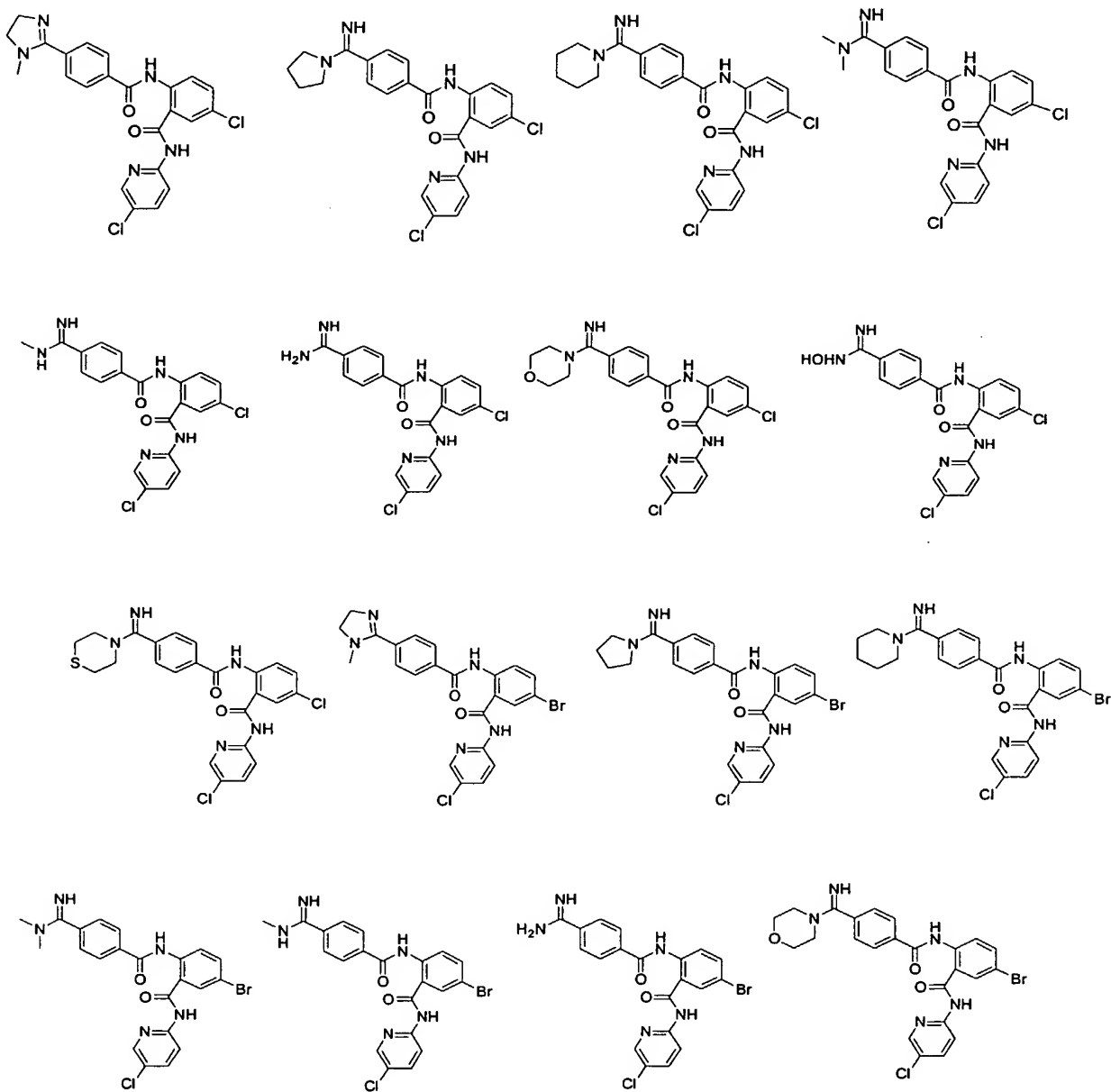
22. The compound according to claim 1 selected from the group consisting of:

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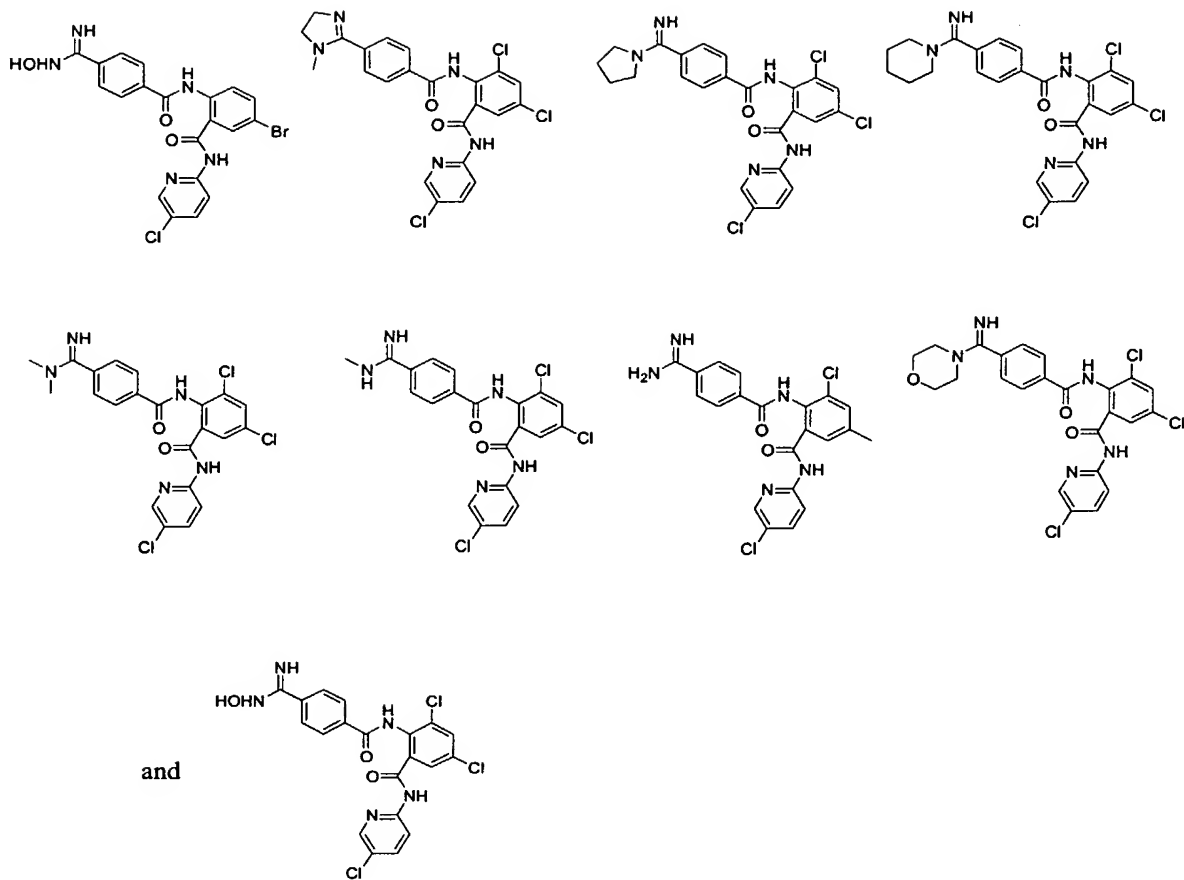


and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

23. The compound according to claim 1 selected from the group consisting of:



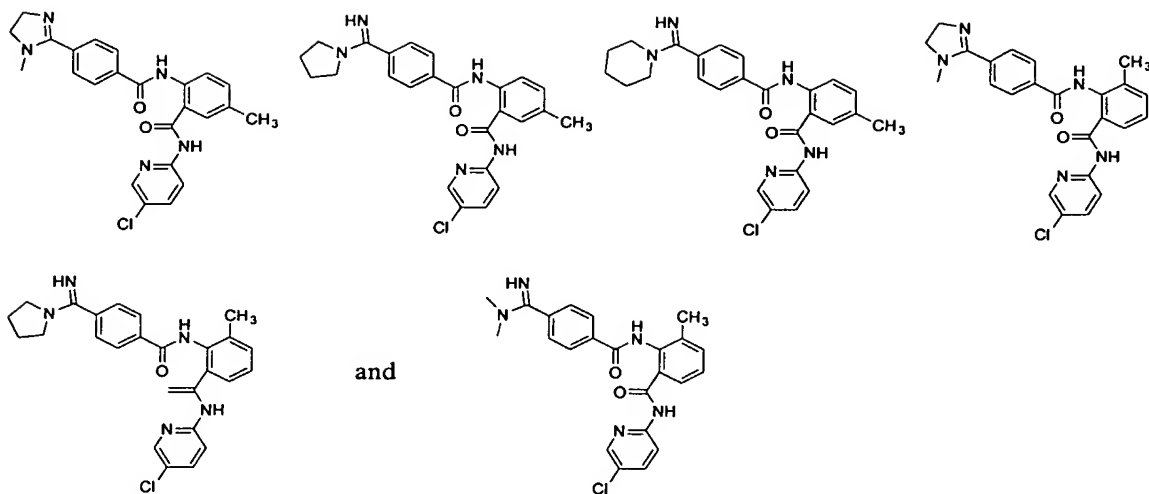
213



- 5 and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

24. The compound according to claim 1 selected from the group consisting of:

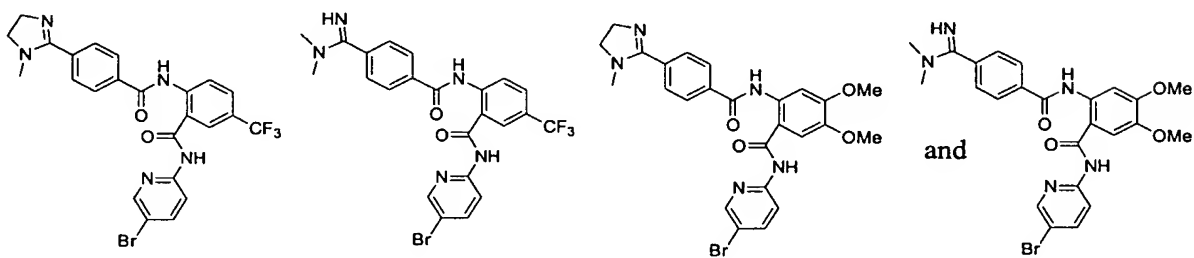
214



and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

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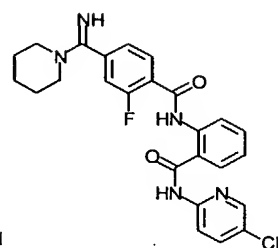
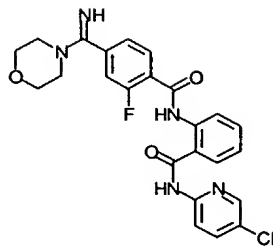
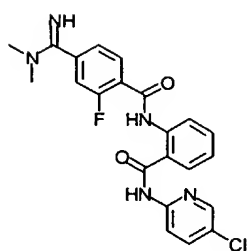
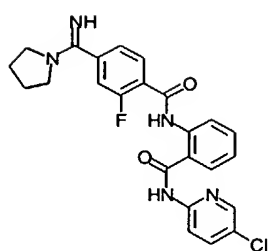
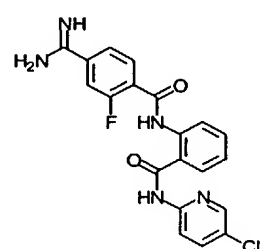
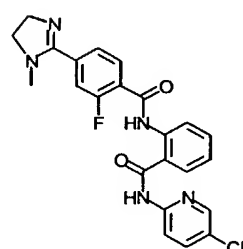
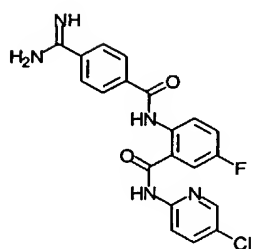
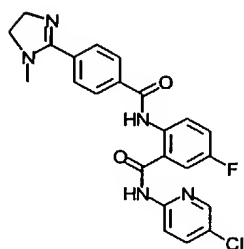
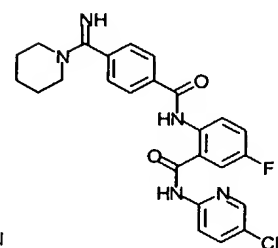
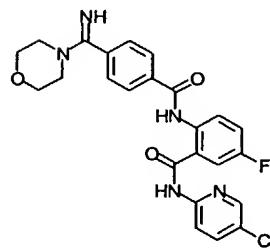
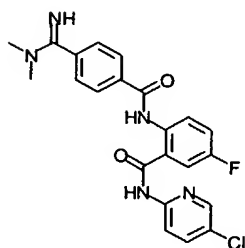
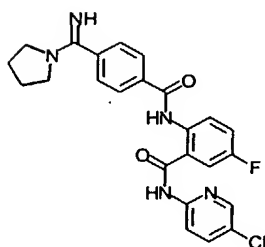
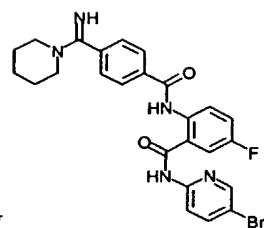
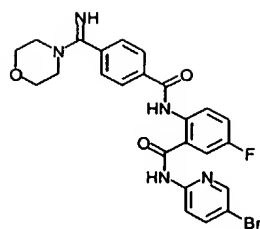
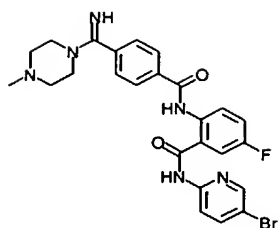
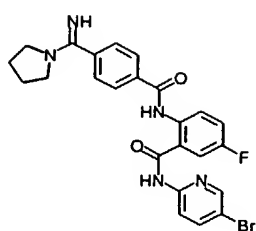
25. The compound according to claim 1 selected from the group consisting of:

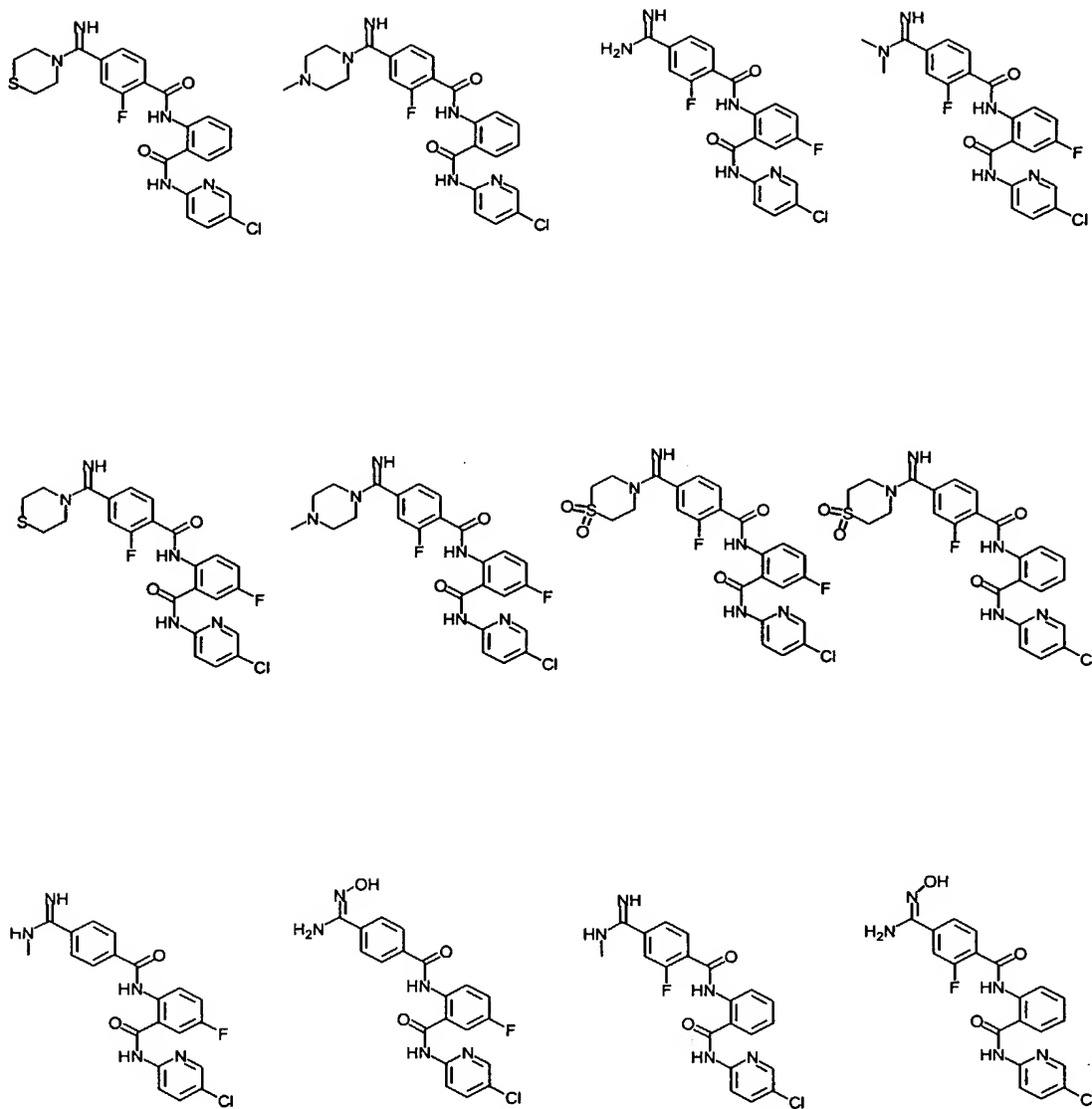


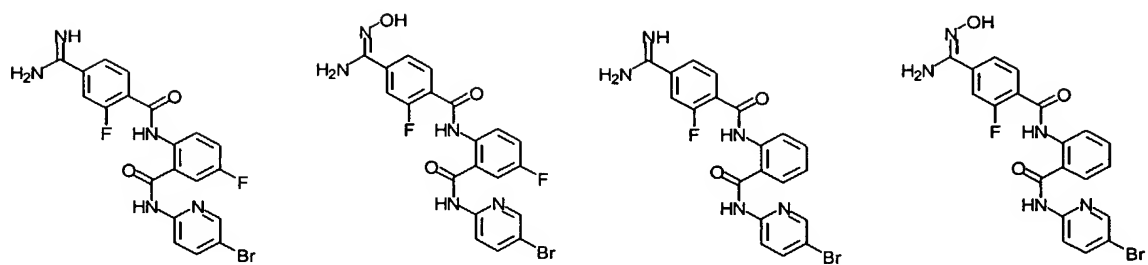
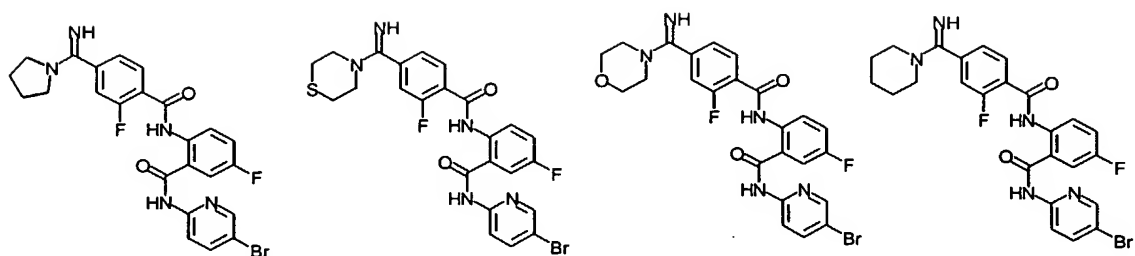
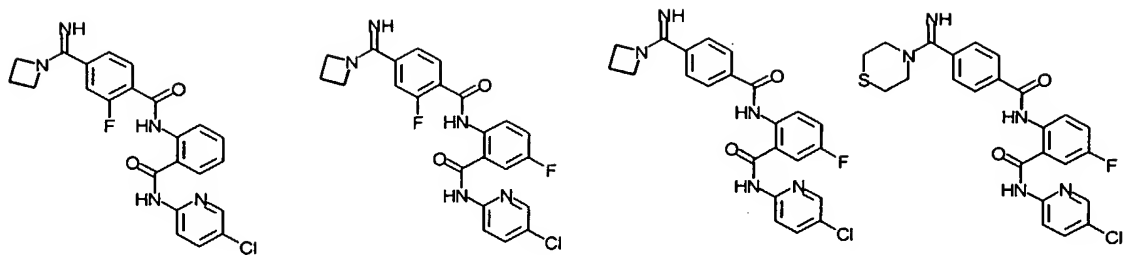
and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

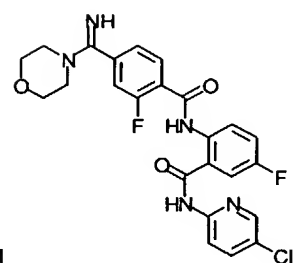
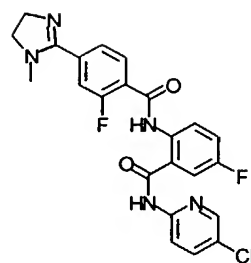
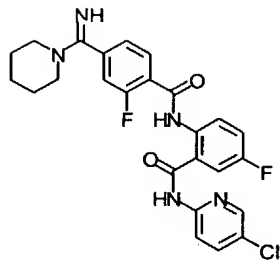
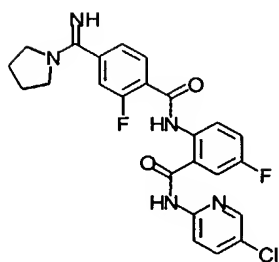
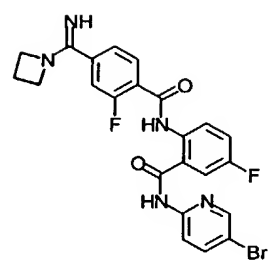
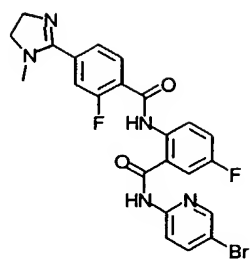
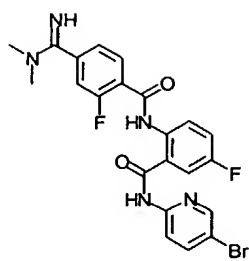
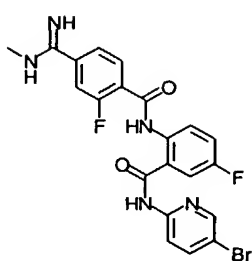
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26. The compound according to claim 1, which is a member selected from the group consisting of:

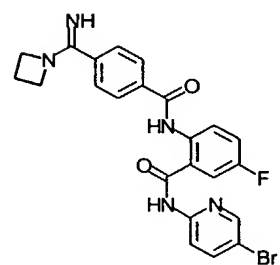
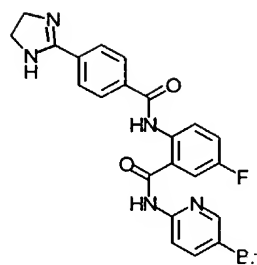
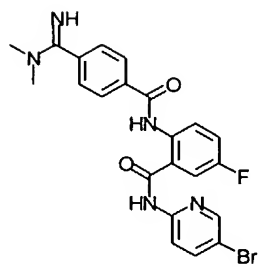
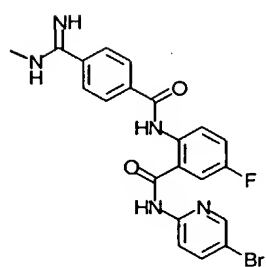




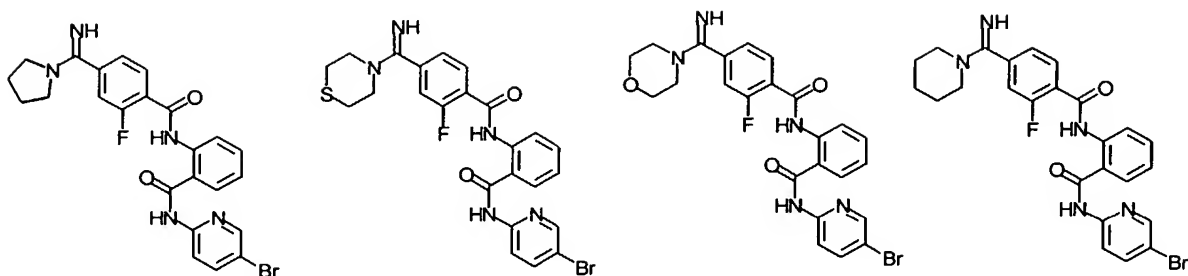




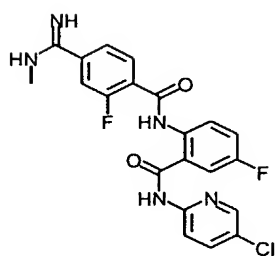
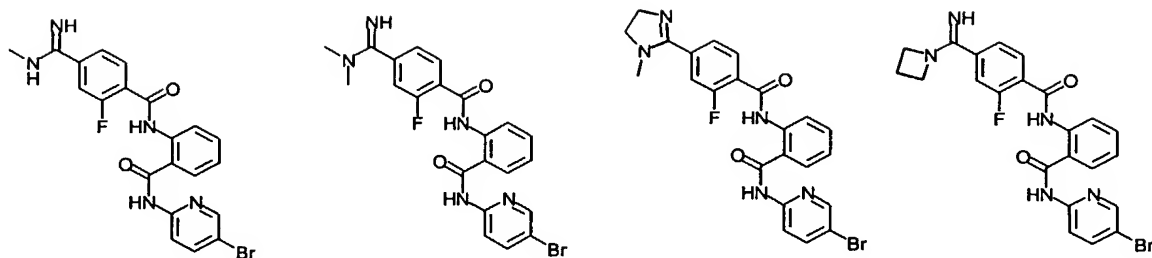
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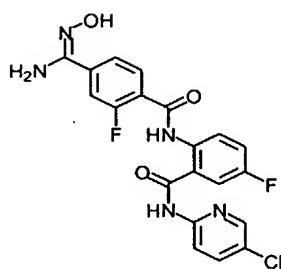
219



5



and



10 and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

27. A pharmaceutical composition for preventing or treating a condition in a

28. A method for preventing or treating a condition in a mammal characterized by undesired thrombosis comprising administering to said mammal a therapeutically effective amount of a compound of claim 1.

29. The method of claim 28, wherein the condition is selected from the group
5 consisting of:

acute coronary syndrome, myocardial infarction, unstable angina, refractory
angina, occlusive coronary thrombus occurring post-thrombolytic therapy or
post-coronary angioplasty, a thrombotically mediated cerebrovascular
syndrome, embolic stroke, thrombotic stroke, transient ischemic attacks,
10 venous thrombosis, deep venous thrombosis, pulmonary embolus,
coagulopathy, disseminated intravascular coagulation, thrombotic
thrombocytopenic purpura, thromboangiitis obliterans, thrombotic disease
associated with heparin-induced thrombocytopenia, thrombotic complications
associated with extracorporeal circulation, thrombotic complications
15 associated with instrumentation, and thrombotic complications associated with
the fitting of prosthetic devices.

30. A method for inhibiting the coagulation of biological samples, comprising the
step of administering a compound of claim 1.

20

31. A pharmaceutical composition for preventing or treating a condition in a
mammal characterized by undesired thrombosis comprising a pharmaceutically
acceptable carrier and a pharmaceutically effective amount of a compound of claim 2.

25 32. A method for preventing or treating a condition in a mammal characterized by
undesired thrombosis comprising administering to said mammal a therapeutically
effective amount of a compound of claim 2.

33. The method of claim 32, wherein the condition is selected from the group consisting of:

5 acute coronary syndrome, myocardial infarction, unstable angina, refractory angina, occlusive coronary thrombus occurring post-thrombolytic therapy or post-coronary angioplasty, a thrombotically mediated cerebrovascular syndrome, embolic stroke, thrombotic stroke, transient ischemic attacks, venous thrombosis, deep venous thrombosis, pulmonary embolus, coagulopathy, disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, thromboangiitis obliterans, thrombotic disease
10 associated with heparin-induced thrombocytopenia, thrombotic complications associated with extracorporeal circulation, thrombotic complications associated with instrumentation, and thrombotic complications associated with the fitting of prosthetic devices.

15 34. A method for inhibiting the coagulation of biological samples, comprising the step of administering a compound of claim 2.

20 35. A pharmaceutical composition for preventing or treating a condition in a mammal characterized by undesired thrombosis comprising a pharmaceutically acceptable carrier and a pharmaceutically effective amount of a compound of claim 3.

25 36. A method for preventing or treating a condition in a mammal characterized by undesired thrombosis comprising administering to said mammal a therapeutically effective amount of a compound of claim 3.

37. The method of claim 36, wherein the condition is selected from the group

post-coronary angioplasty, a thrombotically mediated cerebrovascular syndrome, embolic stroke, thrombotic stroke, transient ischemic attacks, venous thrombosis, deep venous thrombosis, pulmonary embolus, coagulopathy, disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, thromboangiitis obliterans, thrombotic disease associated with heparin-induced thrombocytopenia, thrombotic complications associated with extracorporeal circulation, thrombotic complications associated with instrumentation, and thrombotic complications associated with the fitting of prosthetic devices.

10

38. A method for inhibiting the coagulation of biological samples, comprising the step of administering a compound of claim 3.

15

39. A pharmaceutical composition for preventing or treating a condition in a mammal characterized by undesired thrombosis comprising a pharmaceutically acceptable carrier and a pharmaceutically effective amount of a compound of claim 4.

20

40. A method for preventing or treating a condition in a mammal characterized by undesired thrombosis comprising administering to said mammal a therapeutically effective amount of a compound of claim 4.

41. The method of claim 40, wherein the condition is selected from the group consisting of:

25

acute coronary syndrome, myocardial infarction, unstable angina, refractory angina, occlusive coronary thrombus occurring post-thrombolytic therapy or post-coronary angioplasty, a thrombotically mediated cerebrovascular

thrombocytopenic purpura, thromboangiitis obliterans, thrombotic disease
associated with heparin-induced thrombocytopenia, thrombotic complications
associated with extracorporeal circulation, thrombotic complications
associated with instrumentation, and thrombotic complications associated with
5 the fitting of prosthetic devices.

42. A method for inhibiting the coagulation of biological samples, comprising the
step of administering a compound of claim 4.

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
22 March 2001 (22.03.2001)

PCT

(10) International Publication Number
WO 01/19788 A3

(51) International Patent Classification⁷: **C07C 311/16**,
311/46, 317/40, 317/44, C07D 213/75, 213/81, 213/82,
217/22, 333/38, 401/12, 409/12, 409/14, 417/12, A61K
31/18, 31/33, A61P 7/02

Nimitz Lane, Foster City, CA 94404 (US). **SCARBOROUGH, Robert**; 22 Greenbrier Court, Half Moon Bay, CA 94019 (US).

(21) International Application Number: PCT/US00/25196

(74) Agent: **LEE, Christine, S.**; Morgan, Lewis & Bockius LLP, 1800 M. Street, N.W., Washington, DC 20036-5869 (US).

(22) International Filing Date:
15 September 2000 (15.09.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/154,332 17 September 1999 (17.09.1999) US
60/185,746 29 February 2000 (29.02.2000) US

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

(71) Applicant: **CORTHERAPEUTICS, INC.** [US/US]; 256 E. Grand Avenue, South Francisco, CA 94080 (US).

(72) Inventors: **ZHU, Bing-Yan**; 3325 Adelaide Way, Belmont, CA 94002 (US). **ZHANG, Penglie**; 224 Serrano Drive, South San Francisco, CA 94132 (US). **WANG, Lingyan**; 224 Brentwood Drive, South San Francisco, CA 94080 (US). **HUANG, Wenrong**; 7723 Huntridge Lane, Cupertino, CA 95014 (US). **GOLDMAN, Eric**; 1577 Pershing Drive, #C, San Francisco, CA 94129 (US). **LI, Wenhao**; P.O. Box 1993, South San Francisco, CA 94083 (US). **ZUCKETT, Jingmei**; 130 Barneson Avenue, #1, San Mateo, CA 94402 (US). **SONG, Yonghong**; 1144

Published:
— with international search report

(88) Date of publication of the international search report:
9 August 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: BENZAMIDES AND RELATED INHIBITORS OF FACTOR Xa

(57) Abstract: Compounds of the formula A - Q - D - E - G - J - X in which D is a direct link, a substituted or unsubstituted phenyl or naphthyl group or a heterocyclic ring system; X is a substituted or unsubstituted phenyl or naphthyl group or a heterocyclic system; and the other variables are as defined in the claims, their salts and compositions related thereto having activity against mammalian factor Xa are disclosed. The compounds are useful in vitro or in vivo for preventing or treating coagulation disorders.

WO 01/19788 A3



INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/25196

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07C311/16 C07C311/46 C07C317/40 C07C317/44 C07D213/75
 C07D213/81 C07D213/82 C07D217/22 C07D333/38 C07D401/12
 C07D409/12 C07D409/14 C07D417/12 A61K31/18 A61K31/33

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07C C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BEILSTEIN Data, WPI Data, EPO-Internal, PAJ, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 57934 A (DU PONT MERCK PHARMACEUTICAL) 23 December 1998 (1998-12-23) page 2 -page 8; examples; table 1 ---	1-3, 27-42
X	WO 98 06694 A (DU PONT MERCK PHARMACEUTICAL) 19 February 1998 (1998-02-19) page 2 -page 7; examples; table 1A ---	1-3, 27-42
A	WO 98 28282 A (DU PONT MERCK PHARMACEUTICAL) 2 July 1998 (1998-07-02) page 3 -page 9; examples; table 1 ---	1-42
A	WO 98 28269 A (DU PONT MERCK PHARMACEUTICAL) 2 July 1998 (1998-07-02) page 3 -page 9; examples; table 1A --- -/--	1-42

☒ Further documents are listed in the continuation of box C.

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* Special categories of cited documents :

A document defining the general state of the art which is not considered to be of particular relevance

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O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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* & * document member of the same patent family

Date of the actual completion of the international search

26 February 2001

Date of mailing of the international search report

12/03/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
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 Fax: (+31-70) 340-3016

Authorized officer

ENGLISH, R

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/25196

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61P7/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	J.D. YOUNG, ET AL.: "Interannular interactions in para-substituted diphenylmethane anion redicals" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, vol. 94, no. 25, 13 December 1972 (1972-12-13), pages 8790-8794, XP002161109 American Chemical Society, Washington, DC, US ISSN: 0002-7863 compound 3b --- -/--	1

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- * & * document member of the same patent family

Date of the actual completion of the international search

26 February 2001

Date of mailing of the international search report

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
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Fax: (+31-70) 340-3016

Authorized officer

ENGLISH, R

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/25196

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>H. SUZUKI, ET AL.: "Selective reduction with lithium aluminium hydride / diphosphorus tetraiodide"</p> <p>CHEMISTRY LETTERS, no. 6, June 1983 (1983-06), pages 909-910, XP002161110 Chemical Society of Japan, Tokyo, JP ISSN: 0366-7022 table 1, entries 5,14</p> <p style="text-align: center;">---</p>	1
X	<p>US 2 095 619 A (W.C. STOESEER, ET AL.) 12 October 1937 (1937-10-12) examples 1-6</p> <p style="text-align: center;">---</p>	1
X	<p>S. GOLDSCHMIDT, ET AL.: "Biphenyl derivatives II. Basic 4-biphenyl compounds"</p> <p>RECUEIL DES TRAVAUX CHIMIQUES DES PAYS-BAS., vol. 69, no. 9/10, September 1950 (1950-09), pages 1109-1117, XP002161111 Elsevier Science Publishers, Amsterdam, NL ISSN: 0165-0513 table I</p> <p style="text-align: center;">---</p>	1
X	<p>W.F. COCKBURN, ET AL.: "Molecular rearrangement of tertiary amines. Part I"</p> <p>JOURNAL OF THE CHEMICAL SOCIETY, no. 8, August 1960 (1960-08), pages 3340-3346, XP002161112 Royal Society of Chemistry, Letchworth, GB page 3343, line 4 - line 5</p> <p style="text-align: center;">-----</p>	1

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-3 (in part)

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which part(s) of the claim(s) may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT).

For these reasons it appears impossible to execute a meaningful search and /or to issue a complete search report over the whole breadth of the claim(s). The search and the report for those claims can only be considered complete for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds as indicated in the relevant examples (1-287) and claims 4-26.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/25196

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9857934 A	23-12-1998	AU 7976998 A EP 0993448 A	04-01-1999 19-04-2000
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